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GIULIA ENDERS
illustrations by **Jill Enders**

GUT

The Inside Story of Our Body's Most Underrated Organ

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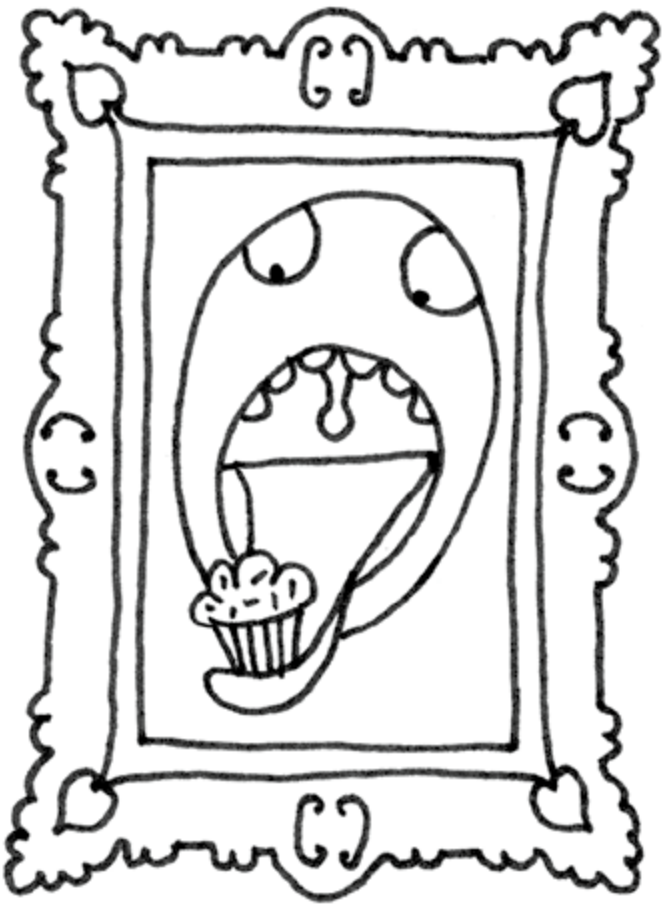

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ILLUSTRATIONS BY JILL ENDERS

Translation by DAVID SHAW

GUT

The Inside Story of Our Body's Most Underrated Organ

GREYSTONE BOOKS

VANCOUVER/BERKELEY

For all single parents who put as much energy and love into bringing up their children as our mother did for my sister and me.

And for Hedi.

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Translation copyright © 2015 by David Shaw
Originally published in Germany as *Darm mit Charme* by Ullstein in 2014
First published in English by Scribe in 2015

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Greystone Books Ltd.www.greystonebooks.com

Cataloguing data available from Library and Archives Canada
ISBN 978-1-77164-149-4 (pbk.)
ISBN 978-1-77164-150-0 (epub)

Editing by Jane Billinghurst
Cover and interior illustrations by Jill Enders
Cover design by Peter Cocking
Distributed in the U.S. by Publishers Group West

We gratefully acknowledge the financial support of the Canada Council for the Arts, the British Columbia Arts Council, the Province of British Columbia through the Book Publishing Tax Credit, and the Government of Canada through the Canada Book Fund for our publishing activities.

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Preface

I WAS BORN BY cesarean section and could not be breast-fed. That makes me a perfect poster child for the intractability of the gastrointestinal tract in the twenty-first century. If I had known more about the gut back then, I could have placed bets on what illnesses I would contract later in life. At first I was lactose intolerant. I never thought about why I was suddenly able to drink milk again at the age of five. At some point I got fat, then thin again. Then, for a long time, I was fine—until I got "the sore."

When I was seventeen, I developed a small sore on my right leg, for no apparent reason. It stubbornly refused to heal, and after a month I went to see my doctor. She didn't really know what it was and prescribed me some cream. Three weeks later, my entire leg was covered in sores. Soon they spread to my other leg, my arms, and my back. Sometimes they appeared on my face. Luckily, it was winter at the time, and everyone thought I had cold sores and a graze on my forehead.

No doctor was able to help me—giving me vague diagnoses of some kind of nervous eczema. They asked me about stress and psychological problems. Cortisone helped a little, but as soon as I stopped using it, the sores just came back. For a whole year, in summer and in winter, I wore tights to stop my sores from weeping through my pants. Then I pulled myself together and started doing some research of my own. By chance, I came across a report about a very similar skin condition. A man had contracted it after taking antibiotics, and I, too, had had to take a course of antibiotics just a couple of weeks before my first sore appeared. It occurred to me that although the sores were on my skin, their appearance might be related to what was going on inside me. Perhaps the course of antibiotics was key? Had they somehow affected my gut?

From that moment on, I ceased to treat my skin like the skin of a person with a dermatological problem and began to see it as the skin of a person with an intestinal condition, though just what that condition might be, I did not know. I decided to cover all the bases. I stopped eating dairy products, cut out gluten almost entirely, swallowed various bacterial cultures, and

generally improved my diet. I also carried out some pretty crazy experiments on myself. If I had already been studying medicine at that time, I wouldn't have dared do half of them. Once, I overdosed on zinc for several weeks, causing me to have an extremely heightened sense of smell for the next few months.

With a few tricks, I finally managed to get my condition under control. This success gave me a lift, and I experienced with my own body that knowledge is power. That's when I started studying medicine.

In my first semester as a student, I was at a party where I ended up sitting next to a guy who had the smelliest breath I have ever smelled. It wasn't a typical bad-breath smell—not the scratchy hydrogen-breath odors of stressed-out middle-aged gentlemen nor the sugary, fetid funk from the mouth of an elderly aunt with too sweet a tooth. After a while, I moved away and sat somewhere else. The next day, he was dead. He had killed himself. I couldn't get him out of my mind. Was there a way his gut might have contributed to this? Just like my skin condition, which at first appeared unrelated? Now I had some experience in medical school, I wondered if it could have been a diseased gut creating that smell, and if so, could a diseased gut also have affected that man's psychological state?

A week later, I decided to share my suspicion with a good friend. And a few months after that, the same friend contracted a bad case of gastroenteritis, which left her feeling very poorly. The next time we met, she told me she thought there might be something in my theory, as her illness had made her feel worse than she ever had felt before, psychologically as well as physically. Her comments inspired me to start looking more closely at this subject matter.

Soon, I discovered there was an entire branch of medical research investigating the links between the gut and the brain. It's a rapidly growing field of study. Ten or so years ago, there were hardly any published studies on the subject; now there are several hundred academic articles covering the field. The influence of the gut on our health and well-being is one of *the* new lines of research in modern medicine. The renowned American biochemist Rob Knight told the journal *Nature* that the field offered at least as much promise as stem cell research. I had stumbled upon a subject I found more and more fascinating.

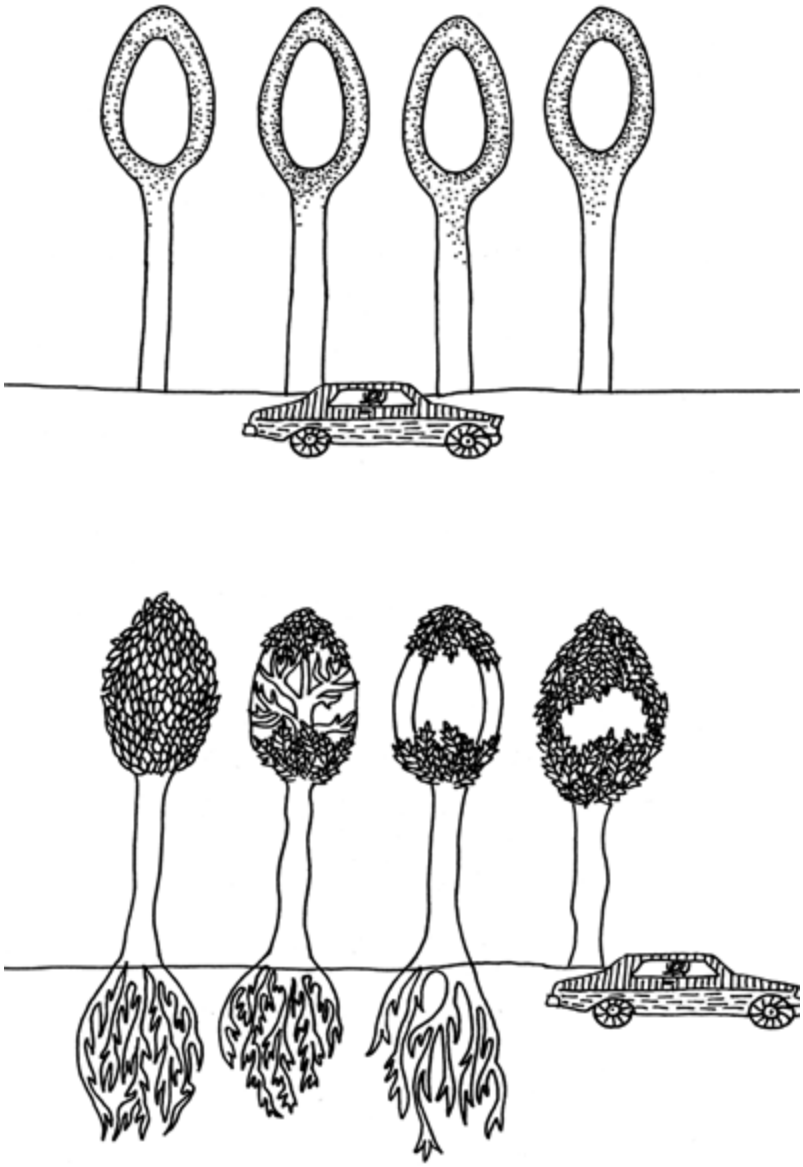
As I continued my medical degree, I got more insight into how my cesarean birth and lack of breast-feeding might have influenced my health later in life. I also realized how neglected, even looked down upon, this area still is in the medical world. This is all the more surprising when you consider what an extraordinary organ the gut is. It accounts for two-thirds of our immune system, extracts energy from sandwiches and vegetarian sausages, and produces more than twenty unique hormones. Most doctors learn very little about this in their training. When I visited the Microbiome and Host Health symposium in Lisbon in May 2013, the number of participants was modest. About half came from institutions with the financial wherewithal to allow them to be among the pioneers, including Harvard, Yale, Oxford, and the European Molecular Biology Laboratory (EMBL) at Heidelberg University.

I'm sometimes shocked by the way scientists huddle behind closed doors to discuss their important research results without informing the public about them at all. Academic caution is often preferable to premature publication, but fear can also destroy opportunities. It is now generally accepted in scientific circles that people with certain digestive problems often suffer from nervous disorders of the gut. Their gut then sends signals to the part of the brain that processes negative feelings, although they have done nothing bad. Such patients feel uneasy but have no idea why. If their doctors simply treat them as irrational mental cases, it can be extremely counterproductive! And this is just one example of why some research results should be published more quickly.

And that is my aim in writing this book. I want to make new knowledge available to a broad audience and communicate the information that scientists bury in their academic publications or discuss behind closed doors at scientific meetings, while many ordinary people out there are searching for answers. I know there are many patients suffering from unpleasant conditions who are frustrated by the medical world. I can't offer any panaceas, and keeping your gut healthy is not a miracle cure for everything, but what I can do is to show, in an entertaining way, why the gut is so fascinating, what exciting new research is currently underway, and how we can use this new knowledge to improve our daily lives.

My medical studies and my doctoral research at the Institute for Medical Microbiology in Frankfurt, Germany, have given me the skills to sift and

sort scientific data. My own personal experience has helped me develop the ability to communicate this knowledge to people. My sister has given me the support I needed to keep me on the right track—listening to me read aloud from my manuscript and saying, with a charming grin, “I think you better try that bit again.”



(PART ONE)

GUT FEELING

THE WORLD IS a much more interesting place if we look beyond what is visible to the naked eye. There is so much more to see! If we start to look more closely, a tree can be more than a spoon-shaped thing. In a highly simplified way, “spoon” is the general shape we perceive when we look at a tree: a straight trunk and a round treetop. Seeing that shape, our eyes tell us “spoon-like thing.” But there are at least as many roots beneath the ground as there are branches above it. Our brain should really be telling us something like “dumbbell,” but it doesn’t. The brain gets most of its input from our eyes, and that information is very rarely in the form of an illustration in a book showing trees in their entirety. So, it faithfully construes a passing forest landscape as “spoon, spoon, spoon, spoon.”

As we “spoon” our way through life like this, we overlook all sorts of wonderful things. There is a constant buzz of activity beneath our skin. We are perpetually flowing, pumping, sucking, squeezing, bursting, repairing, and rebuilding. A whole crew of ingenious organs works so perfectly and efficiently together that, in an adult human being, they require no more energy than a 100-watt light bulb. Each second, our kidneys meticulously filter our blood—much more efficiently than a coffee filter—and in most cases they carry on doing so for our entire lives. Our lungs are so cleverly designed that we use energy only when we breathe in. Breathing out happens without any expenditure of energy at all. If we were transparent, we would be able to see the beauty of this mechanism: like a wind-up toy car, only bigger, softer, and more lung-y. While some of us might be sitting around thinking “Nobody cares about me!”, our heart is currently working its seventeen-thousandth twenty-four-hour shift—and would have every right to feel a little forgotten when its owner thinks such thoughts.

If we could see more than meets the eye, we could watch as a clump of cells grows into a human being in a woman’s belly. We would suddenly see how we develop, roughly speaking, from three tubes. The first tube runs right the way through us, with a knot in the middle. This is our cardiovascular system, and the central knot is what develops into our heart. The second tube develops more or less parallel to the first along our back. Then it forms a bubble that migrates to the top end of our body, where it stays put. This tube is our nervous system, with the spinal cord, including the brain, at the top and myriad nerves branching out into every part of our

body. The third tube runs through us from end to end. This is our intestinal tube—the gut.

The intestinal tube provides many of the furnishings of our interior. It grows buds that bulge out farther and farther to the right and left. These buds will later develop into our lungs. A little bit lower down, the intestinal tube bulges again and our liver has begun to develop. It also forms our gall bladder and pancreas. But, most importantly, the tube itself begins to grow increasingly clever. It is involved in the complex construction of our mouth, creates our esophagus, with its ability to move like a break dancer, and develops a little stomach pouch so we can store food for a couple of hours. And, last but not least, the intestinal tube completes its masterpiece—the eponymous intestine or gut.

The masterpieces of the other two tubes—the heart and the brain—are generally held in high regard. We see the heart as central to life since it pumps blood around the body. The brain is admired for its ability to create a dazzling array of new mental images and concepts every second. But the gut, in most people's eyes, is good for little more than going to the toilet. Apart from that, people think, it just hangs around inside our bellies, letting off a little "steam" every now and then. People do not generally credit it with any particular abilities. It would be fair to say that we underestimate our gut. To put it more bluntly, we don't just underestimate it, we are ashamed of it—more "guilt feeling" than "gut feeling"!

I hope this book will change that by making use of the wonderful ability that books possess to show us more than the world we see around us. Trees are not spoons, and the gut is our body's most underrated organ. This is its inside story.

How Does Pooping Work? And Why That's an Important Question

MY FLATMATE WANDERED into the kitchen one day, saying, "Giulia, you study medicine—so how does pooping work?" It probably wouldn't be a great idea for me to begin my autobiography with that question, but that little query did literally change my life. I withdrew to my room, sat on the floor, and was soon poring over three different textbooks. The answer I eventually discovered left me flabbergasted. This unspectacular daily necessity turned out to be far more sophisticated and impressive than I ever would have imagined.

Every time we go to the toilet, it's a masterly performance—two nervous systems working tirelessly in tandem to dispose of our waste as discreetly and hygienically as possible. Very few other animals do their business in such an admirable and orderly manner. Our bodies have developed all sorts of mechanisms and techniques to help us poop properly. The first surprise is the sophistication of our sphincters. The vast majority of people are familiar only with the outer sphincter: the muscle we can consciously control, opening and closing it at will. There is another, very similar muscle close by—but this is one we can't control consciously.

Each of the two sphincters looks after the interests of a different nervous system. The outer muscle is a faithful servant of our consciousness. When our brain deems it an unsuitable time to go to the toilet, the external sphincter obeys and stays closed with all its might. The internal sphincter represents our unconscious inner world. Whether Great-Aunt Bertha approves of breaking wind or not is no concern of the *sphincter ani internus*. It is only interested in making sure everything is okay inside us. Is the gas pressure rising? The inner sphincter's mission is to keep all unpleasantness at bay. If it had its way, Great-Aunt Bertha would break wind more often. The main thing for the internal sphincter is to keep everything comfortable and in its place.

These two sphincter muscles have to work as a team. When what's left of our food reaches the internal sphincter, that muscle's reflex response is to

open. But it does not just open the floodgates and let everything out, leaving the outer sphincter to deal with the deluge. First, it allows a small “taster” through. The space between the internal and external sphincter muscles is home to a large number of sensor cells. They analyze the product delivered to them, test it to find out whether it is solid or gaseous, and send the resulting information up to the brain. This is the moment when the brain realizes, “It’s time to go to the toilet!” Or maybe, “It’s just a bit of wind.” It then does what it is so good at with its conscious awareness: it adapts to the environment we find ourselves in. It compares the information it receives from our eyes and ears to the data in its memory bank of past experience. In this way, the brain takes just a matter of seconds to make an initial assessment of the situation and send a message back to the sphincter: “I’ve had a look and we’re at Great-Aunt Bertha’s, in the living room. We might get away with breaking a little wind if we can squeeze it out silently—anything more solid might not be such a good idea.”

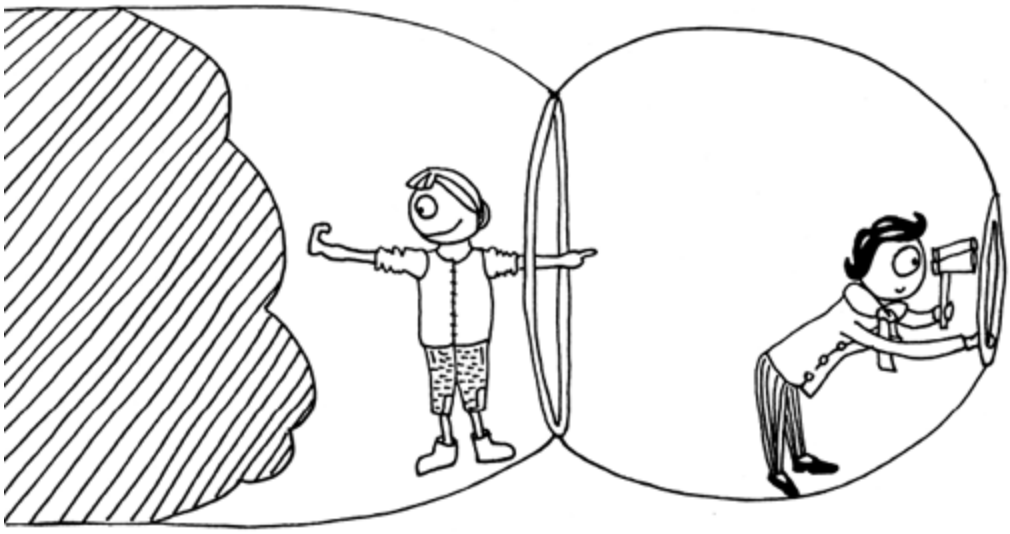
The external sphincter gets the message and dutifully squeezes itself closed even more tightly than before. The internal sphincter receives this signal from its more outgoing partner and respects the decision—for now. The two muscles work together and maneuver the taster back into a holding pattern. Of course, it will have to come out sooner or later, just not here and not now. After a while, the internal sphincter will simply give it a try with another little taster. If by then we’re back within our familiar four walls, it’s full steam ahead!

Our internal sphincter is a no-nonsense little guy. His motto is “If it’s gotta come out, it’s gotta come out!” Not much room for argument there. The external sphincter, on the other hand, has to deal with the vagaries of the outside world and its many options. It might, theoretically, be possible to use this stranger’s toilet, but is that a good idea? Have my new girlfriend/boyfriend and I been together long enough for farting in front of each other to be okay—and if so, is it down to me to break the ice and go first? If I don’t go to the toilet now, can I wait until this evening or will I get caught short?

The considerations of our sphincter may not sound worthy of a Nobel Prize, but in fact they are concerned with some of the most basic questions of human existence: how important to us is our inner world, and what compromises should we make to get by in the external world? There are

those who clench with all their might to keep the wind in, come what may, eventually struggling home wracked with bellyache. Others get Granny to pull on their finger at a family party, making a funny, if slightly inappropriate, magic show out of their need to break wind. The best compromise is probably somewhere in the middle.

If we suppress our need to go the toilet too often or for too long, our internal sphincter begins to feel browbeaten. In fact, we are able to reeducate it completely. That means the sphincter and the surrounding muscles have been disciplined so often by the external sphincter that they become cowed. If communication between the two sphincters breaks down completely, constipation can result.



Even without such defecatory discipline, something very similar can happen to women during labor. Childbirth can cause tearing of the delicate nerve fibers that allow the two muscles to communicate with each other. The good news is that those nerves can heal and reconnect. Irrespective of whether the damage was caused by childbirth or in some other way, one good treatment option is what doctors call biofeedback therapy. Biofeedback therapy is offered by some gastroenterologists or gastroenterology departments. It teaches the two sphincters to overcome their estrangement and get to know each other again. A machine is used to measure how efficiently the internal and external sphincters are working together. If messages from one to the other get through, the patient is rewarded with a sound or light signal. It’s like one of those quiz shows on

early-evening television, where the whole set lights up and fanfares blare when a contestant gets the answer right—only it's at a medical practice, not on television, and the "contestant" has a sensor electrode up his or her butt. That may seem extreme, but it's worth it. When the two sphincters are talking properly to each other again, going to the little girls' or little boys' room is an altogether more pleasant experience.

Sphincters, sensor cells, consciousness, and electrode-up-the-butt quiz shows. My flatmate was probably not expecting all that in answer to his casual question about pooping, nor did the group of rather prim female business studies students who had meanwhile gathered in the kitchen for his birthday party. Still, the evening turned out to be fun, and it made me realize that a lot of people are actually interested in the gut. Some interesting new questions were raised at the birthday party. Is it true that we don't sit on the toilet properly? How can we burp more easily? Why can we get energy from steaks, apples, or fried potatoes, for example, but cars are much more restricted in their fuel options? Why do we have an appendix? Why are feces always the same color?

My flatmates have learned to recognize the familiar look on my face when I rush into the kitchen, bursting to tell them my latest gut anecdote—like the one about the tiny squat toilets and luminous poop.

Are You Sitting Properly?

It's a good idea to question your own habits from time to time. Are you really taking the shortest and most interesting route to the bus stop? Is that comb-over to hide your increasing bald patch elegant and chic? Or, indeed, are you sitting properly when you go to the toilet?

There will not always be a clear, unambiguous answer to every question, but a little experimentation can sometimes open up whole new vistas. That is probably what was going through the mind of Dov Sikirov when the Israeli doctor asked twenty-eight test subjects to do their daily business in three alternative positions: enthroned on a normal toilet; half-sitting, half-squatting on an unusually low toilet; and squatting with no seat beneath them at all. He recorded the time they took in each position and asked the

volunteers to assess the degree of straining their bowel movements had required. The results were clear. In a squatting position, the subjects took an average of 50 seconds and reported a feeling of full, satisfactory bowel emptying. The average time when seated was 130 seconds and the resulting feeling was deemed to be not quite so satisfactory.

Why the difference? The closure mechanism of our gut is designed in such a way that it cannot open the hatch completely when we are seated. There is a muscle that encircles the gut like a lasso when we are sitting or, indeed, standing, and it pulls the gut in one direction, creating a kink in the tube. This mechanism is a kind of extra insurance policy, in addition to our old friends, the sphincters. Some people will be familiar with this kinky closing mechanism from their garden hose. You ask your sister to check why there's no water coming out of the hose. When she peers down the end, you quickly unbend the kink, and it's just a few minutes until your parents ground you for a week.

But back to our kinky rectal closure mechanism: it means our feces hit a corner. Just like a car on the highway, turning a corner means our feces have to put on the brakes. So, when we are sitting or standing, our sphincters have to expend much less energy keeping everything in. If the lasso muscle relaxes, the kink straightens, the road ahead is straight, and the feces are free to step on the gas.

Squatting has been the natural defecation position for humans since time immemorial. The modern sitting toilet has existed only since indoor sanitation became common in the late eighteenth century. But such "cavemen did it that way" arguments are often met with disdain by the medical profession. Who says that squatting helps the muscle relax better and straightens the feces highway? Japanese researchers fed volunteers luminous substances and X-rayed them while they were doing their business in various positions. They found out two interesting things. First, squatting does indeed lead to a nice, straight intestinal tract, allowing for a direct, easy exit. Second, some people are nice enough to let researchers feed them luminous substances and X-ray them while they have a bowel movement, all in the name of science. Both findings are pretty impressive, I think.

Hemorrhoids, digestive diseases like diverticulitis, and even constipation are common only in countries where people generally sit on some kind of

chair to pass their stool. This is due not to lack of tissue strength, especially in young people, but to the fact that there is too much pressure on the end of the gut. Some people tend to tense up all their abdominal muscles when they are stressed. Often, they don't even realize they are doing it. Hemorrhoids prefer to avoid internal pressure like that by dangling loosely out of the anus. Diverticula are small light-bulb-shaped pouches in the bowel wall, resulting from the tissue in the gut bulging outward under pressure.

Of course, the way we go to the toilet is not the only cause of hemorrhoids and diverticula; however, it remains a fact that the 1.2 billion people in this world who squat have almost no incidence of diverticulosis and far fewer problems with hemorrhoids. We in the West, on the other hand, squeeze our gut tissue until it comes out of our behinds and we have to have it removed by a doctor. Do we put ourselves through all that just because sitting on a throne is more "civilized" than silly squatting? Doctors believe that straining too much or too often on the toilet can also seriously increase the risk of varicose veins, a stroke, or defecation syncope—fainting on the toilet.

A text message I received from a friend who was on holiday in France read, “The French are crazy! Someone’s stolen the toilets from the last three service stations we stopped at!” I had to laugh, first, because I suspected my friend was actually being serious, and second, because it reminded me of my first experience of French squat toilets. “Why am I being forced to squat here when you could just as easily have put in a proper toilet?” I mournfully complained to myself as I recovered from the shock of the emptiness I saw before me. Throughout much of Asia, Africa, and southern Europe people squat briefly over such toilets in a kind of martial arts or downhill skiing

pose to defecate. We, by contrast, take so long, we have to while away the time until we've finished our business with reading the paper, carefully prefolding pieces of toilet paper for imminent use, scanning the corners of the bathroom to see if they could do with a clean, or staring patiently at the opposite wall.

When I read this chapter out to my family in our living room, I looked up to see disconcerted faces. Are we going to have to descend from our porcelain thrones and squat precariously over a hole to poop? Of course not, hemorrhoids or no hemorrhoids! That said, it might be fun to try climbing up onto the toilet seat to do our business while squatting there. But there's no need for that, either. It is possible to squat while sitting. It's a particularly good idea when things don't come so easily, so to speak. To do it, just incline your upper body forward slightly and put your feet on a low footrest placed in front of the toilet, et voilá!—all the angles are correct, and you can read the paper, prefold your tissue, or stare at the wall with a clear conscience.

The Gateway to the Gut

YOU MIGHT THINK that the back end of the gut has so many surprises in store for us because it is something we do not think about very much. But I don't think that's the real reason. The other end of the gut, the gateway, so to speak, also has no shortage of surprises in store—even though we are directly confronted with it every morning when we clean our teeth.

You can seek out these secrets with your tongue. These are four small points in your mouth. Two of them are located on the inside of your cheeks, opposite your upper molars, more or less in the middle. If you explore the area with your tongue, you will feel two tiny bumps. If they notice them at all, most people assume they must have bitten themselves in the cheek at some point, but they haven't. These little nubs, which doctors call the parotid papillae, are found in the same position in everybody's mouth. The other two points are lurking beneath your tongue, just to the right and left of the lingual frenulum, the fold of skin connecting your tongue to the floor of your mouth. These four little nubs supply your mouth with saliva.

The papillae in your cheeks secrete saliva whenever it's needed right away—for example, when we eat. The two tiny openings under the tongue secrete saliva continuously. If you could somehow enter these channels and swim against the tide of saliva, you would eventually reach the main salivary glands. They produce the most saliva—about 1½ to 2 US pints (0.7 to 1 liter) a day. If you feel upward from your neck to your cheek, you will notice two soft, round raised areas. May I introduce you? They are the bosses.

THE SUBLINGUAL PAPILLAE, those two constant suppliers of saliva, are situated right behind our lower front teeth, which are particularly susceptible to the buildup of tartar. This is because there are substances in our saliva that contain calcium whose sole function it is to make our teeth harder. But if a tooth is constantly bombarded with calcium, it can be a case of too much of a good thing. Tiny molecules floating innocently by are caught up and “fossilized” without so much as a by-your-leave. The problem is not the tartar itself, but the fact that it has such a rough surface, affording a much better foothold for bacteria that cause tooth decay and gum disease than smooth, clean tooth enamel.

But what are fossilizing, calcium-containing substances doing in our saliva? Saliva is basically filtered blood. The salivary glands sieve the blood, keeping back the red blood cells, which are needed in our arteries, not in our mouth. But calcium, hormones, and some products of our immune system enter the saliva from the blood. That explains why each person’s saliva is slightly different. In fact, saliva analysis can be used to test for diseases of the immune system or for certain hormones. The

salivary glands can also add extra substances, including those calcium-containing compounds, and even natural painkillers.

Our saliva contains one painkiller that is stronger than morphine. It is called opiorphin and was only discovered in 2006. Of course, we produce only small amounts of this compound, otherwise we would be spaced out on our own spit all the time! But even a small amount has a noticeable effect, since our mouth is such a sensitive thing. It contains more nerve endings than almost anywhere else in the human body. Even the tiniest strawberry seed can drive us crazy if it gets stuck somewhere. We feel every grain of sand in a badly washed salad. A teeny little sore, which we would not even notice if it were on our elbow, hurts like hell and feels monstrously big in our mouth—without our salivary painkiller, it would feel even worse!

When we chew, we produce more saliva and with it more of such analgesic substances, which explains why a sore throat often feels better after a meal and even minor sores in the oral cavity hurt less. It doesn't have to be a meal—even chewing gum provides us with a dose of our oral anodyne. There are even a handful of new studies showing that opiorphin has antidepressant properties. Is our spit partly responsible for the reassuring effects of comfort eating? Medical research into both pain and depression may deliver the answers in the next few years.

Saliva protects the oral cavity not only from too much pain, but also from too many bad bacteria. That's the job of mucins, for example. Mucins are proteins that form the main constituent of mucus. They help provide hours of fascination and fun for young children who have just found out they can blow bubbles with their own spit. A more useful function is their ability to envelop our teeth and gums in a protective mucin net. We shoot them out of our salivary papillae like Spider-Man shoots webs from his wrists. These microscopic nets can catch bacteria before they have a chance to harm us. While the bad bacteria are caught in the net, antibacterial substances in our saliva can kill them off.

Like the natural painkillers in our saliva, bactericidal substances are present in our saliva in small concentrations. Our spit is not supposed to disinfect us completely. In fact, we actually need a core team of good little creatures in our mouth. Benign bacteria in the mouth are not totally wiped out by our disinfectant saliva since they take up space—space that could otherwise be populated by more dangerous germs.

When we are asleep, we produce very little saliva. That's good news for those who tend to drool into their pillow. If they produced the full daytime quota of 2 to 3 US pints (1 to 1.5 liters) during the night, too, the results would not be particularly pleasant. The fact that we produce so little saliva at night explains why many people have bad breath or a sore throat in the morning. Eight hours of scarce salivation means one thing for the microbes in our mouth—party time! Brazen bacteria are no longer kept in check, and the mucus membranes in our mouth and throat miss their sprinkler system.

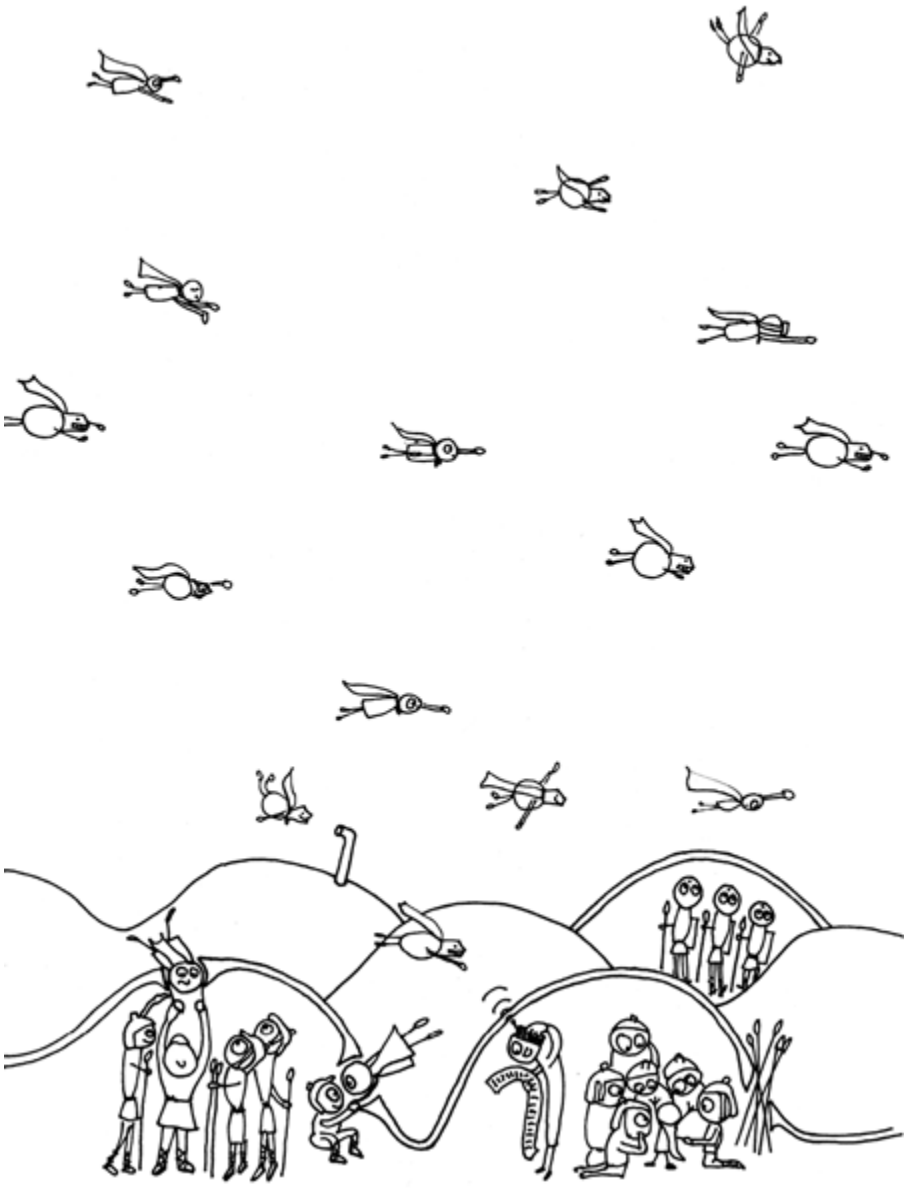
That is why brushing your teeth before you go to bed at night and after you get up in the morning is such a clever idea. Brushing at bedtime reduces the number of bacteria in your mouth, leaving fewer partygoers for the all-night bash. Brushing in the morning is like cleaning up after the party the night before. Luckily, our salivary glands wake up at the same time we do in the morning and start production straight away. Munching on our first piece of toast or performing our morning dental hygiene duties adds extra stimulation for salivation, and this washes away the nocturnal microbes or transports them down into our stomach, where our gastric juices finish them off.

Those who suffer from bad breath during the day may have not managed to remove enough musty-smelling bacteria. Those cunning little critters love to hide out under the newly formed mucin net, where the antibacterial substances in our saliva cannot get to them. A tongue scraper can help here, but so can chewing gum, which helps stimulate saliva production to swill out those mucin hideouts. If none of this helps, there is another place where the causes of bad breath can lurk—but more of that later, after we have found out about the second secret place in our mouth.

This place is one of those typical surprises—like when you think you know someone, only to find out they have an unexpected crazy side to them. The well-coiffed secretary from Chicago who turns up on the Internet as a fanatical ferret breeder. The heavy-metal guitarist seen buying skeins of yarn because he finds knitting so relaxing and it's such a good workout for the fingers. The best surprises come after first impressions have been made, and the same is true of your own tongue. When you look in the mirror and stick out your tongue, you are not seeing it in all its glory. You might well ask how it looks farther down, as you can clearly see that it does not just

end at the back of your mouth. In fact, the root of the tongue is where things start to get really interesting.

The root of the tongue is home to an alien landscape of pink domes. Those whose gag reflex is not too pronounced can carefully feel the root of their tongue with a finger. When you reach the root, you will notice it gets pretty bumpy back there. The job of these nodules—doctors call them your lingual tonsils—is to investigate everything we swallow. To do this, they pick up tiny particles of anything we eat, drink, or inhale and draw them into the nodule. Inside, an army of immune cells waits to receive training in how to deal with foreign substances invading from the outside world. They need to learn to leave bits of apple in peace, while attacking anything that might give us a sore throat. So, if you do explore the root of your tongue with your finger, it is not clear who is explorer and who the explored. After all, this area includes some of the most inquisitive tissue in our body—immune tissue.



The immune tissue at the base of the tongue, also called the lingual tonsils.

The immune tissue has a number of such inquisitive hotspots. Strictly speaking, a ring of immune tissue encircles our entire throat. Known to scientists as Waldeyer’s tonsillar ring, it includes those lingual tonsils at the bottom of the circle; the palatine tonsils—these are the ones we generally think of as our tonsils—at either side; and at the top of the ring, where the ear, nose, and throat areas meet, there is more such tissue. (When swollen and infected, especially in children, this is what we know as adenoids.)

Those who believe they have no tonsils left are not quite correct. The entire collection of tissue in Waldeyer's ring makes up our tonsils. Whether they are located at the root of the tongue, at the back of the mouth, or at the side of our throat, all these areas of tonsillar tissue do the same job: they inquisitively investigate any foreign substance they encounter and use the information to train the immune system to defend us.

The tonsils—the ones we often have removed—are just not as clever in the way they go about this task. Rather than forming bumps, they tend to form deep grooves (to increase surface area) known rather spookily as "crypts." Sometimes, too much foreign material can get caught in the crypts, leading to frequent infections. This is a side effect, so to speak, of having overinquisitive tonsils. So, if the tongue and teeth have been excluded as a cause of a patient's bad breath, the next place to check is the tonsils—if they are still there.

Sometimes, little white stones can be found hiding in the crypts, and these stones smell terrible! Often, people have no idea they are there, and they spend weeks trying unsuccessfully to get rid of bad breath or a strange taste in their mouth. No amount of tooth brushing, tongue scraping, or gargling helps. The little stones will eventually work their way out of their hiding places, with no permanent harm done. But you can also take fate into your own hands and, with a little practice, squeeze them out. That done, bad breath problems disappear instantaneously.

The best test to find out whether smelly breath is caused by these little deposits is simply to run a finger or a cotton bud over the tonsils and then sniff it. If it smells unpleasant, it is time to go hunting for tonsil stones. Ear, nose, and throat doctors can also remove them, which is the safer and more convenient option. Those with a strong stomach and a love of barely watchable videos can visit YouTube to see various techniques for squeezing tonsil stones out and view some extreme examples. But be warned! These videos are not for the fainthearted.

There are also other household remedies for tonsil stones. Some people gargle with salt water several times a day; others swear by fresh, raw sauerkraut from the health-food store; and yet others claim cutting out dairy products will prevent them from forming. There is no scientific basis for any of these remedies. A more thoroughly researched medical question is

that of when a tonsillectomy can or should be carried out. The answer turns out to be—not before the age of seven.

Seven is the age by which we have probably seen it all, or all that is important for our immune cells: being born into a completely unfamiliar world; being kissed and cuddled by Mom; playing in the garden or the woods; touching animals; having many colds in quick succession; meeting a load of new people at school. And that's about it. By this time, our immune system has finished its schooling, so to speak, and can go to work for us for the rest of our life.

Before we reach the age of seven, our tonsils are still an important training camp for our immune cells. Building a healthy immune system is not only important for warding off colds, it also has an important part to play in keeping our heart healthy and in controlling our body weight. For example, removing the tonsils of a child younger than seven can lead to an increased risk of obesity. Why this should be the case is something doctors have not yet discovered. However, more and more researchers are now becoming interested in the link between the immune system and body weight. This tonsil-tubbiness effect can be a boon for underweight children because the associated weight gain can propel them into the normal weight range, but for all other children, parents are best advised to make sure their child eats a healthy, balanced diet after a tonsillectomy.

So the tonsils of children below the age of seven should stay in, unless there is a very good reason for taking them out. If the tonsils are so large that they impede normal breathing or sleeping, for example, the tonsil-tubbiness effect is secondary. It may seem sweet of our immune tissue to want to defend us so loyally, but in such cases, it does more harm than good. Often, doctors can use lasers to remove only that part of the tonsils that is causing the trouble. They no longer have to leave patients completely tonsil-less. Chronic or repeated infections are a different story altogether. In such cases, our immune cells are kept constantly busy, with no time for a bit of R&R, and that is not good for them if it continues for too long. Whether we are four, seven, or fifty years old, an oversensitive immune system can benefit from saying goodbye to those tonsils.

One example of those who benefit from having their tonsils removed is psoriasis sufferers. In psoriasis, an overreaction of the immune system causes itchy skin lesions—often starting at the head—and painful

inflammation of the joints. Psoriasis patients also have an above-average vulnerability to sore throats. One possible factor in this is bacteria, which can hide in the tonsils for long periods of time and needle the immune system from there. For more than thirty years, doctors have described cases of psoriasis patients whose skin condition improved or cleared up entirely following a tonsillectomy. In 2012, this prompted researchers from Iceland and the United States to investigate the phenomenon more closely. They split twenty-nine psoriasis patients who also suffered frequent sore throats into two groups. One group had their tonsils surgically removed, the other didn't. Thirteen of the fifteen "detonsilized" patients reported a significant long-term improvement in their skin. Those still in possession of their tonsils reported little or no change. Some sufferers of rheumatic diseases are also now advised to have their tonsils removed if they are suspected of being part of the cause of the condition.

Tonsils in or tonsils out? There are good arguments for both. Those forced to bid farewell to their tonsils at an early age need not worry that their immune system has missed an important lesson from the oral cavity. Luckily, there is still all the rest of the tissue at the base of the tongue and back of the throat. And those whose tonsils are still in place need not worry that they have been left with nothing but a trap for bacteria. Many people's tonsillar crypts are quite shallow and so are less likely to cause problems for their owners. The other parts of Waldeyer's ring are actually very bad at providing a refuge for bacteria: they are constructed differently and have glands to help them clean themselves regularly.

There is something happening every second in our mouth: salivary papillae shoot out nets of mucin, take care of our teeth, and protect us from the effects of oversensitivity. Our tonsillar ring keeps watch for foreign particles and uses them to train its immune army. But we would need none of this if the story didn't continue beyond our mouth. The mouth is simply the gateway to a world where the external becomes internalized.

The Structure of the Gut

SOME THINGS TURN out to be a disappointment once you get to know them better. Those chocolate wafers from the television commercial are not lovingly hand-baked by housewives in country dresses—they come from a factory with neon strip lighting and workers at production lines. School turns out to be much less fun than you thought it would be on the first day. It's warts and all in the backstage area of life, where there is a lot that looks much better from a distance than up close.

That is not the case for the gut, however. Our intestinal tube looks rather odd from a distance. Beyond the mouth, a 1-inch- (2-centimeter-) wide esophagus, or gullet, leads down from the throat, misses the top of the stomach, and passes into it somewhere at the side. The right-hand side of the stomach is much shorter than the left, which is why it curls up into a crescent-shaped, lopsided pouch. The small intestine meanders with no particular sense of direction, sometimes to the right, sometimes to the left, for all its length (about 20 feet, or 6 meters) until it eventually passes into the large intestine. That's where we find the apparently useless appendix, which seems to be incapable of doing anything except getting infected. The large intestine is also full of bulges. In fact, it looks a little like a sorry attempt to replicate a string of beads. Seen from a distance, the gut is an unsightly, charmless, asymmetrical tube.

So, let's forget the view from a distance and zoom in for a closer look. There is scarcely another organ in our body that becomes increasingly fascinating the closer you get. And, the more you know about the gut, the more beautiful it appears. So, let's look at some of those strange structures a little more closely.

The Lanky Esophagus

The first thing we notice about this long, slender organ is that it can't aim properly. Rather than taking the shortest route and aiming for the middle of the stomach, it enters the organ on the right-hand side. This is a smart move. Surgeons would call such a connection terminolateral. It may mean taking a little detour, but it's well worth it. When simply walking normally, we tense our abdominal muscles, doubling the pressure in our abdomen with every step we take. When we laugh or cough, for example, that pressure increases by several times. Since the abdomen presses against the stomach from below, it would be a bad idea for the esophagus to dock directly onto the top end of the stomach. Connected as it is at the side, it has to deal with only a fraction of the pressure. It is thanks to this arrangement that we can take a walk after a heavy meal without having to burp with every step. This clever angle and its closing mechanism are also to thank for the fact that, although a fit of laughter might result in us losing a little control over our outer sphincter and inadvertently letting out a little "laughing gas," few people have been known to vomit from laughing.

A side effect of this lateral connection is the so-called gastric bubble. This small bubble of air at the top of the stomach can be seen clearly on X-rays. Air rises vertically, after all, and does not search out a side exit. This bubble is the reason many people find they have to swallow a little air in order to burp. This swallowing motion moves the opening of the esophagus a little closer to the bubble, and—hey presto!—the burp can make its upward journey to freedom. Those who need to burp while lying down can make the process easier by lying on their left side. So, if you're kept awake at night by a bloated stomach and you are lying on your right side, the best thing to do is simply to turn over.

The lanky appearance of the esophagus is also more beautiful than it seems at first glance. Looking very closely, it can be seen that some muscle fibers run around the esophagus in a spiral pattern. They are the reason for its elasticity. If you extend these fibers lengthways, they constrict spirally, like a telephone receiver cable. Bundles of fibers connect the esophagus to the spinal column. Sitting up straight and looking upwards stretches the esophagus along its length. This causes it to narrow, in turn allowing it to close more efficiently at each end. That is why sitting or standing up straight can help prevent heartburn after a large meal.

In order better to illustrate the stomach bubble, this illustration does not show the correct distribution of black and white in a normal X-ray image. Normally, denser materials, such as teeth or bone, show up white, while less dense materials, such as the stomach bubble or the air in the lungs, show up as dark areas.

The Lopsided Stomach Pouch

Our stomach sits much higher in our abdomen than we think. It begins just below the left nipple and ends below the bottom of the ribcage on the right. Any pain felt farther down than this lopsided little pouch cannot be stomachache. Often, when people say they have stomach problems, the trouble is actually in the gut. The heart and the lungs sit on top of the stomach. This explains why we find it more difficult to breathe deeply after eating a lot.

One condition often overlooked by general practitioners and family doctors is Roemheld syndrome, when so much gas collects in the stomach that it presses up against the heart and the nerves in the gut. Sufferers can display a range of different symptoms, including dizziness and discomfort. In more severe cases, Roemheld syndrome can cause anxiety or difficulty in breathing, and may also lead to severe chest pain that feels like a heart attack. Doctors often write off undiagnosed Roemheld sufferers as overanxious malingerers whose symptoms are all in their mind. A more useful approach would be to ask patients if they have tried burping or passing wind. In the long term, it may be better for such patients to avoid any food that leaves them bloated or flatulent, take measures to restore the balance of the stomach or gut flora, and avoid drinking alcohol to excess. Alcohol can multiply the number of gas-producing bacteria by a factor of up to a thousand. In fact, some bacteria feed on alcohol (which is why rotten fruit tastes alcoholic). With a gut full of busy gas producers, a night on the town can lead to a morning chorus of the pungent kind. So much for the “alcohol is a disinfectant” argument!

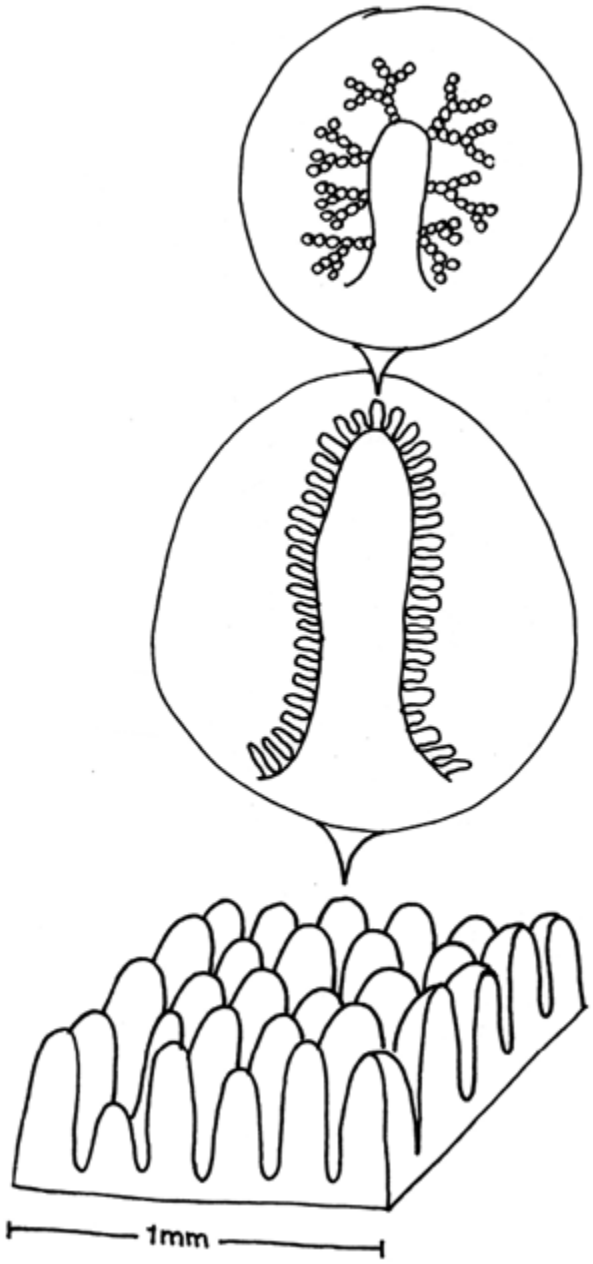
Now let us turn to the stomach’s strange shape. One side is much longer than the other and so the entire organ has to bend double. That creates large folds inside it. The stomach could be called the Quasimodo of the digestive organs. But its misshapen appearance has a deeper meaning. When we take a drink of water, the liquid can flow straight down the shorter, right-hand side of the stomach to end up at the entrance to the small intestine. Food, on the other hand, plops against the larger side of the stomach. Our digestive pouch cunningly separates the substances it still needs to work on to break them down, from the fluids that it can wave straight on through to the next digestive station. So our stomach is not simply lopsided; rather, it has two sides with different specializations. One side copes better with fluids, the other with solids. Two stomachs for the price of one, so to speak.

The Meandering Small Intestine

The small intestine meanders about in our abdominal cavity, twisting and turning for a distance of between 10 and 20 feet (3 and 6 meters). If we bounce on a trampoline, it bounces along with us. When the plane we're sitting on takes off, it is pressed into the back of the seat like the rest of us. When we dance, it merrily wobbles along to the music, and when abdominal pain makes us wince, its muscles wince in a similar way.

There are few people in the world who have seen their own small intestine. Even doctors usually examine only the large intestine when they perform a colonoscopy. But those who do get the rare opportunity of seeing their small intestine by swallowing a pill-sized camera are likely to be surprised. Most expect to encounter a gloomy tunnel, but what they see is a very different creature: moist, pink, with a velvety sheen and somehow delicate looking. Most people do not realize that only the final three feet or so (about the last meter) of our large intestine has anything to do with feces —the preceding sections of our intestinal tract are surprisingly clean (and largely smell-free, incidentally). Our gut faithfully and tastefully takes on everything we swallow down to it.

At first sight, the small intestine seems rather more haphazard in its design than our other organs. The heart has its four chambers, the liver has its lobes, veins have valves, and the brain has specialized areas—but the small intestine just wanders aimlessly about in our abdomen. Its true design becomes clear at the microscopic level. We have here a creature that epitomizes the phrase "love of detail."



Intestinal villi, microvilli, and glycocalyxes. One millimeter (mm) is slightly less than 1/16 of an inch.

Our gut wants to offer us as much surface area as possible. That is why it loves folds—including the folds we can see with the naked eye. Without folds, our small intestine would need to be up to 60 feet (18 meters) long to provide us with enough surface area for our digestion. So, here's to folds! But a perfectionist like the small intestine doesn't stop there. Each square inch of its surface contains about 20,000 tiny fingerlike projections (or

about 30 projections per square millimeter). These projections, called villi by scientists, protrude out into the mush of partly digested food, the medical word for which is “chyme.” The villi’s size means they appear as a velvety structure to the unaided human eye. Under the microscope, the little villi look like large waves made out of cells. (Velvet looks very similar under a microscope.) Even greater magnification reveals that each and every one of those cells is itself covered with little protrusions—the microvilli: villi on villi, if you like. The microvilli are, in turn, covered with a velvety meshwork made of countless sugar-based structures that look a little bit like antlers. These are called the glycocalyxes. If all this—the folds, the villi, and the microvilli—were ironed out to a smooth surface, our small intestine would have to be some 4½ miles (7 kilometers) long.

Why does the small intestine have to be so huge, anyway? In total, the surface area of our digestive system is about one hundred times greater than the area of our skin. That seems a little excessive just to deal with a small portion of fries or a single apple. But this is what it’s all about inside our belly: we enlarge ourselves as much as possible in order to reduce anything from outside to the smallest size we can, until it is so tiny that our body can absorb it and it eventually becomes a part of us.

We begin that process in the mouth. A bite of an apple sounds like such a juicy idea because, when we take that bite, our teeth burst millions of apple cells like tiny balloons. The fresher the apple is, the more of its cells remain intact—which is why we can tell how fresh the fruit is by its crispness as we bite into it.

Just as we prefer crisp, fresh fruit, we also love hot, protein-rich food. We find steak, scrambled eggs, or fried tofu more appetizing than raw meat, slimy eggs, or cold bean curd. That’s because we have an intuitive understanding of how digestion works. If we swallow a raw egg, it will undergo the same processes in our stomach as it would in the frying pan. The white of the egg turns opaque, the yolk takes on a pastel color, and both set and become solid. If we were to vomit the raw egg back up after the right amount of time, the results would look like almost perfect scrambled eggs—without any cooking! Proteins react to the heat in the hot pan and the acid in our stomach in the same way—they unfold. That means they no longer possess the clever design features that make them soluble in the liquid of the egg white, so they form solid white lumps. In this state, they

can be digested far more easily in the stomach and the small intestine. Cooking food saves us the whole first burst of energy required to unfold those proteins, which would otherwise have to be expended by the stomach. By preferring cooked food, the body outsources the first part of the digestive process.

The final breakdown of the food we eat takes place in the small intestine. Right at the start of this part of the gut there is a small opening in its wall. This is the duodenal papilla—similar to the salivary papillae in our mouth, but bigger. It is through this little hole that digestive juices are squirted onto the chyme. As soon as we eat something, the liver and pancreas begin to produce these juices and deliver them to the papilla. These juices contain the same agents as the laundry detergent and dish soap you can buy from any supermarket: digestive enzymes and fat solvents. Laundry detergent is effective in removing stains because it "digests out" any fatty, protein-rich, or sugary substances from your laundry, with a little help from the movement of the washing-machine drum, leaving these substances free to be rinsed down the drain with the dirty water. That is more or less the same as what happens in our small intestine. The main difference is that the pieces of protein, fat, or carbohydrates that are broken down in the intestine ready to be transported to the bloodstream through the gut wall are huge by comparison. A bite of an apple is then no longer a bite of apple, but a nutritious pulp made up of billions and billions of energy-rich molecules. Absorbing them all requires a huge surface area—a length of 4½ miles (7 kilometers) is just about enough. That also leaves some space as a safety buffer, in case parts of the gut are temporarily put out of action by infection or gastric flu.

Each individual villus contains a tiny blood vessel—a capillary—that is fed with the absorbed molecules. All the small intestine's blood vessels eventually come together and carry the blood to the liver, where the nutrients are screened for harmful substances and toxins. Any dangerous substances can be destroyed here before the blood passes into the main circulatory system. If we eat too much, this is where the first energy stores are created. The nutrient-rich blood then flows from the liver directly to the heart. There, it receives a powerful push and is pumped to the countless cells of our body. In this way, a sugar molecule can end up in a skin cell in your right nipple, for example, where it is absorbed and then "burned"

along with oxygen. That releases energy, which the cell uses to stay alive, with heat and tiny amounts of water created as by-products. This happens inside so many cells at the same time that the heat produced keeps our body at a constant temperature of 97 to 99 degrees Fahrenheit (36 to 37 degrees Celsius).

The basic principle underlying our energy metabolism is simple. Nature requires energy to ripen an apple on the tree. We humans come along and break the apple down into its constituent molecules and metabolize them for energy. We then use the energy released to keep us alive. All the organs that develop out of that embryonic gut tube are able to provide fuel for our cells. Our lungs, for example, do nothing other than absorb molecules with every breath we take. Thus, “breathing in” really means “taking in nourishment in gaseous form.” A good proportion of our body weight is made from such inhaled atoms and not from cheeseburgers. Indeed, plants draw the majority of their weight from the air and not from the soil they grow in... I hope I haven’t just inadvertently provided the next dubious diet idea to appear in women’s magazines!

So, all our body’s organs use up energy, but it is from the small intestine that we start to get some energy back. That explains why eating is such a pleasant pastime. However, we can’t expect to feel a burst of energy as soon as we have swallowed the last mouthful of a meal. In fact, many people find they feel tired and sluggish after eating. The food has not yet reached the small intestine—it is still in the preparatory stages of digestion. We no longer feel hungry because our stomach has been expanded by the food we’ve eaten. But we feel just as sluggish as we did before the meal, and now we have to come up with the extra energy for all that mixing and breaking down. To achieve this, a large amount of blood is delivered to our digestive organs, and many researchers also believe that postprandial tiredness may be due to the resulting reduced blood supply to the brain.

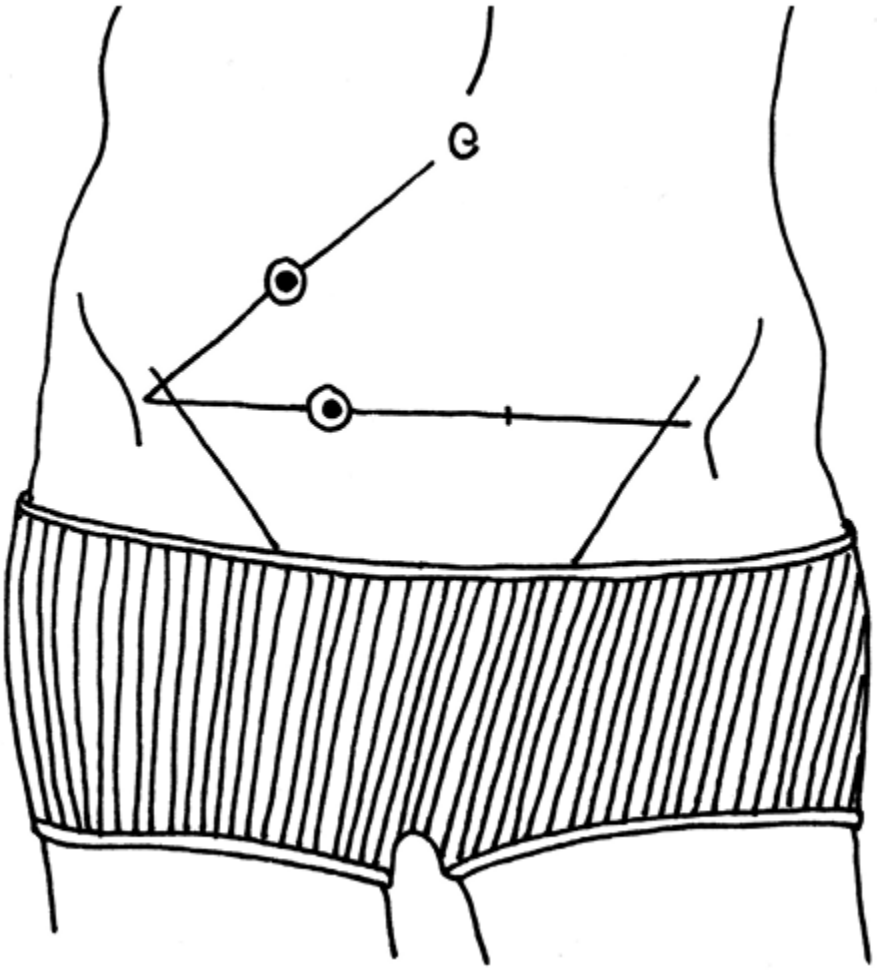
One of my professors always dismissed that idea, arguing that if all the blood in our head were diverted to our stomach we would be dead, or at least unconscious. Indeed, there are other possible causes of the fatigue that follows eating. Certain messenger chemicals released by the body when we are full can also stimulate the areas of the brain responsible for tiredness. This tiredness is perhaps inconvenient for our brain when we are at work, but the small intestine welcomes it. It works most effectively when we are

pleasantly relaxed. It means the optimum amount of energy is available for digestion and our blood is not full of stress hormones. The phlegmatic after-lunch reader is a more efficient digester than the stressed-out office executive.

The Unnecessary Appendix and the Bulgy Large Intestine

There are nicer things in life than lying on an examining table at the doctor's with one thermometer in your mouth and another in your behind. But that used to be the standard examination in cases of suspected appendicitis. A significantly higher temperature down below than in the mouth was a major indication. Modern doctors no longer need to rely on temperature differences to diagnose appendicitis. Important symptoms are fever in combination with pain below and to the right of the belly button (the position of the appendix in most people).

Often, pressing that side of the lower abdomen will cause pain, while, curiously, pressing the other side will relieve it. As soon as pressure on the left-hand side is released—ouch! This is because our abdominal organs are surrounded by a supporting fluid. When pressure is applied to the left-hand side, extra support fluid is pushed over to the right, where it provides additional cushioning for the inflamed gut, which relieves pain. Other signs of appendicitis are pain when raising the right leg against a resistant pressure (get someone to push against it), lack of appetite, and nausea.



Our appendix, officially known as the vermiform, or worm-shaped, appendix, has a reputation for being useless. Looking like a deflated balloon of the kind children's party entertainers twist into animal shapes, the appendix is not only too small to deal with chyme, it is also positioned in a location that partly digested food hardly ever reaches. It is just below the junction between the small and large intestines, and is completely bypassed. This is a creature that can only look on from below as the world continues on its way above. Those of you who remember the bumpy landscape in your mouth might have an idea what its true function could be. Although far removed from the rest of its kind, the appendix is part of the tonsillar immune tissue.

Our large intestine takes care of things that cannot be absorbed in the small intestine. For that reason, it does not have the same velvety texture. It

would simply be a waste of energy and resources to fill this part of the gut with absorbent villi. Instead, the large intestine is the home of most of our gut bacteria, which can break down the last nutritious substances for us. And our immune system is very interested in these bacteria.

So, the vermiform appendix couldn't be better placed. It is far enough away so as not to be bothered by all the digestive business going on above it, but close enough to monitor all foreign microbes. Although the walls of the large intestine include large deposits of immune cells, the appendix is made almost entirely of immune tissue. So, if a bad germ comes by, it is surrounded. However, that also means that everything around it can become infected—360-degree, panoramic inflammation, so to speak. If this inflammation causes the appendix to swell, the little tube has problems sweeping itself clean of those bad germs—leading to one of the more than 270,000 appendectomies carried out every year in the United States alone.

However, that is not the only function of the appendix. It leaves only good germs alive and attacks anything it sees as dangerous, and this also means a healthy appendix acts as a storehouse of all the best, most helpful bacteria. This was discovered by American researchers Randal Bollinger and William Parker in 2007. Its practicality comes into play after a heavy bout of diarrhea. That will often flush away many of the typical gut microbes, leaving the terrain free for other bacteria to settle. This should not be left to chance. And this is when, according to Bollinger and Parker, the appendix team steps in and spreads out protectively throughout the entire large intestine.

In most parts of North America and northern Europe, we do not have many pathogens that cause diarrhea. We may pick up a gastrointestinal flu bug every now and then, but our environment teems with much less dangerous microbes than in India or Spain, for example. So you could say that we do not need our appendix as urgently as the people in those regions. That means no one in areas with few diarrhea-inducing pathogens who has undergone an appendectomy, or is about to face one, should be too worried. The immune cells in the rest of the large intestine may not be quite so closely packed, but in total, they are many times more numerous than those in the appendix, and they are competent enough to take on the job. Anyone who wants to take no chances after a bout of diarrhea can buy good bacteria at the pharmacy to repopulate their gut.

So now, I hope, it is clear why we have an appendix. But what's the purpose of the large intestine that it is appended to? Nutrients have already been absorbed, there are no villi here, and what does our gut flora want with indigestible leftovers anyway? Our large intestine does not wind about like its smaller counterpart. It surrounds our small intestine on the outside, like a plump picture frame. And it would not take exception to being called plump—it simply needs more room to do its job.

"Waste not, want not" may sound hackneyed today, but for past generations it was a way to survive lean times. And it is also the motto of our large intestine. It takes its time with all the leftovers and digests them thoroughly. The small intestine can get on with processing the next meal, or even the next two, in the meantime, without affecting the large intestine's work. It doggedly processes leftovers for sixteen hours or so. In doing so, it makes available substances that would have been lost if the gut were more hurried. They include important minerals like calcium, which can only be absorbed properly here. The careful cooperation of the large intestine and its flora also provides us with an extra helping of energy-rich fatty acids, vitamin K, vitamin B12, thiamine (vitamin B1), and riboflavin (vitamin B2). Those substances are useful for many things—for example, to help our blood clot properly, to strengthen our nerves, or to prevent migraines. In the final three feet or so (about the last meter) of the large intestine, our water and salt levels are finely tuned. Not that I'm recommending a taste test, but the saltiness of our feces always remains the same. This fine-balancing act saves the body an entire quart (or liter) of fluids, which we would have to make up by drinking that much more per day.

As with the small intestine, all the treasures absorbed by the large intestine are transported first to the liver for checking, before entering the main blood system. The final few inches (or centimeters) of the large intestine, however, do not send their blood to the detoxifying liver; blood from their vessels goes straight into the main circulatory system. This is because, generally, nothing more is absorbed in this section, simply because everything useful has already been removed. But there is one important exception: any substances contained in a medical suppository. Suppositories can contain much less medication than pills and still take effect more quickly. Tablets and fluid medications often have to contain large doses of the active agent because much of it is removed by the liver before it even

reaches the area of the body it is meant to act on. That is, of course, less than ideal, since the substances recognized by the liver as toxins are the reason we take the medicine in the first place. So, if you want to do your liver a favor and still need to take fever-reducing or other medication, make use of the shortcut via the rectum and use a suppository. This is an especially good idea for very young or very old patients.

What We Really Eat

THE MOST IMPORTANT phase of our digestion takes place in the small intestine, where the maximum surface area meets the maximum reduction of our food down to the tiniest pieces. This is where the decisions are made. Can we tolerate lactose? Is this food good for our health? Which food causes allergic reactions? Here, in this final stage of breakdown, our digestive enzymes work like tiny pairs of scissors. They snip away at our food until it shares a lowest common denominator with our cells. Canny as ever, Mother Nature here makes use of the fact that all living things are made out of the same basic ingredients: sugar molecules, amino acids, and fats. Everything we eat comes from living things—at this biological level, there is no difference between an apple, a tree, and a cow.

Sugar molecules can be linked to form complex chains. When that happens, they no longer taste sweet, and we know them as the carbohydrates we find in bread, pasta, or rice. After that piece of toast you ate for breakfast has undergone the snipping of the enzyme scissors, the final product is the same number of sugar molecules as a couple of spoonfuls of refined household sugar. The only difference is that household sugar does not require so much work from our enzymes as it is already broken down into such small pieces when it arrives in the small intestine that it can be absorbed directly into the bloodstream. Eating too much pure sugar at once really does make our blood sweeter for a while.

The sugar contained in white toast is digested relatively quickly by our enzymes. With wholegrain bread, everything moves at a much more leisurely pace. Such bread contains particularly complex sugar chains, which have to be broken down bit by bit. So, wholegrain bread is not a sugar explosion, but a beneficial sugar store. Incidentally, our body has to work much harder to restore a healthy balance if a sugar onrush comes suddenly. It pumps out large amounts of various hormones, most importantly insulin. The result is that we rapidly feel tired again once this special operation is over. If it doesn’t enter the system too quickly, sugar is an important raw material for our body. It is used as fuel for our cells—like

heat-giving firewood—or to build sugar structures for use in our body, such as the antler-like glycocalyxes attached to our gut cells.

Despite the problems, our body loves sugary sweet treats because they save the body work, since sugar can be taken up more quickly. The same is true of warm proteins. In addition, sugar can be turned into energy extremely quickly, and our brain rewards us for a rush of rapid energy by making us feel good. However, there is one problem: never before, in the history of humankind, have we been faced with such a huge abundance of readily available sugar. Some 80 percent of the processed foods found on the shelves of modern-day American supermarkets contain added sugar. On an evolutionary scale, then, we could say our species has just discovered the secret stash of candies at the back of the cupboard, and it keeps returning to binge on the booty before collapsing on the couch with a stomachache and sugar shock.

Even though we know intellectually that too much snacking is bad for us, we can't really blame our instincts for encouraging us to grab every opportunity for a treat. When we eat too much sugar, our body simply stores it away for leaner times. Quite practical, really. One way the body does this is by relinking the molecules to form long, complex chains of a substance called glycogen, which is then stored in the liver. Another strategy is to convert the excess sugar into fat and store it in fatty tissue. Sugar is the only substance our body can turn into fat with little effort.

Glycogen reserves are soon used up—just about the time during your run when you notice the exercise is suddenly much harder work. That is why nutritional physiologists say we should do at least an hour's exercise if we want to burn fat. It is not until we pass through that first energy dip that we start to tap into those fine reserves. We might find it annoying that our paunch isn't the first thing to go, but our body is deaf to such complaints. The simple reason for this is that human cells adore fat.

Fat is the most valuable and efficient of all food particles. The atoms are so cleverly combined that they can concentrate twice as much energy per ounce as carbohydrates or protein. We use fat to coat our nerves—just like the plastic on an electric cable. It is this coating that makes us such fast thinkers. Some of the most important hormones in our body are made out of fat, and every single one of our cells is wrapped in a membrane made largely of fat. Such a special substance must be protected and not

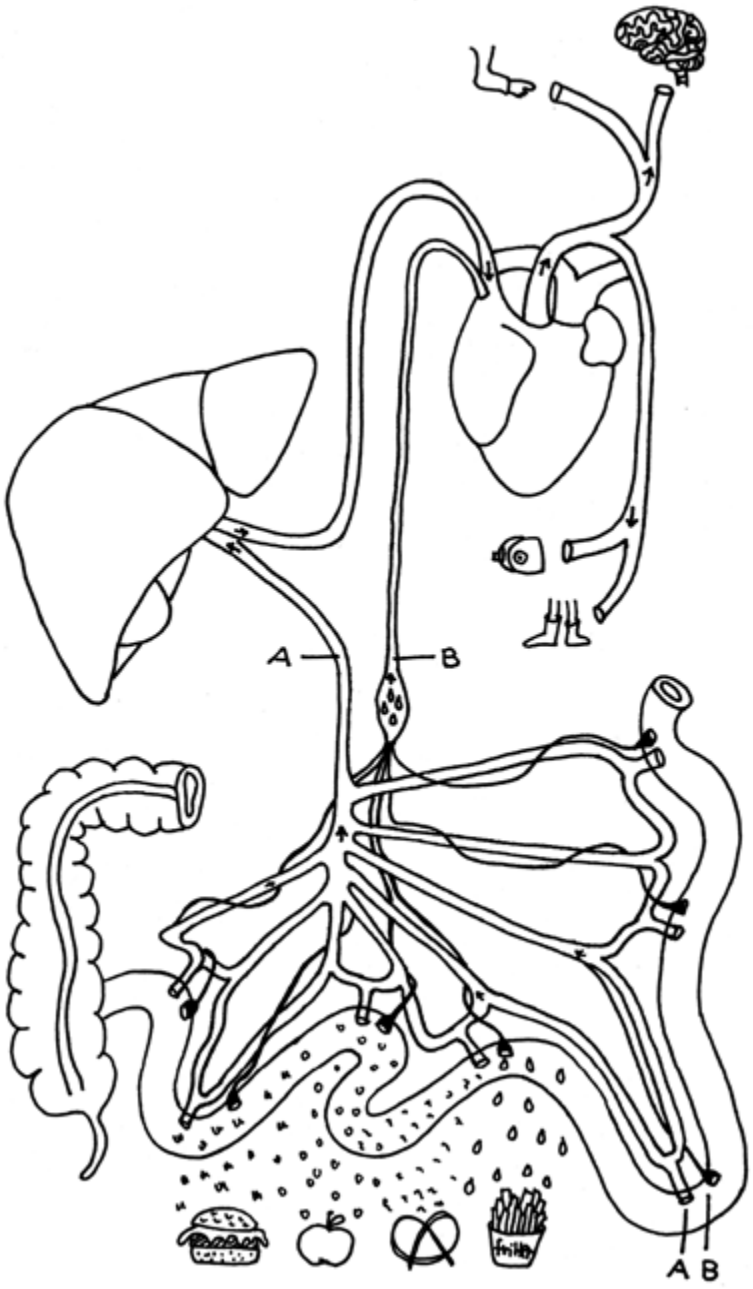
squandered at the first sign of physical exertion. When the next period of famine comes—and there have been many over the eons—every ounce of fat in that paunch is a life insurance policy.

Our small intestine also knows the special value of fat. Unlike other nutrients, it cannot be absorbed straight into the blood from the gut. Fat is not soluble in water—it would immediately clog the tiny blood capillaries in the villi of the gut and float on top of the blood in larger vessels, like the oil on spaghetti water. So fat must be absorbed via a different route: the lymphatic system. Lymphatic vessels are to blood vessels as Robin is to Batman. Every blood vessel inside the body is accompanied by a lymphatic vessel, even each tiny capillary in the small intestine. While our blood vessels are thick and red and heroically pump nutrients to our tissues, the lymphatic vessels are thin and filmy white in color. They drain away fluid that is pumped out of our tissue and transport the immune cells, whose job it is to ensure that everything is as it should be throughout the body.

Lymphatic vessels are so slight because they do not have muscular walls like our blood vessels. Often, they work just by using gravity. That explains why we sometimes wake up in the morning with swollen eyes. Gravity is not very much help when you are lying down. The tiny lymphatic vessels in our face are nicely open, but it is only when we get up and gravity kicks in that the fluid transported there during the night by our blood vessels can flow back down. (The reason our lower legs do not fill up with fluid after a long day on our feet is that our leg muscles squeeze the lymphatic vessels every time we take a step and that squeezes the fluid—known as lymph in medical circles—upwards.) The lymphatic system is seen as an under-appreciated weakling everywhere in the body except in the small intestine. This is its time to shine! All the body's lymph vessels converge in an impressively thick duct, where all the digested fat can gather without the risk of clogging.

It's well known that doctors like to show off their Latin skills, and they give this vessel the mighty sounding name *ductus thoracicus.* It sounds almost as if it means to say, "Hail, Ductus! Teach us why noble fat is so important and evil fat so bad!" Shortly after we eat a fatty meal, there are so many tiny fat droplets in our *ductus* or thoracic duct that the lymph fluid is no longer transparent but milky white. When the fat has gathered, the thoracic duct skirts the belly, passes through the diaphragm, and heads

straight for the heart. (All the fluid drained from our legs, eyelids, and gut ends up here.) So, whether it's extra virgin olive oil or cheap fat from french fries, it all goes straight into the heart—there is no detoxing detour via the liver as there is for everything else we digest.



A = Blood vessels pass through the liver and then go on to the heart.
B = Lymphatic vessels go straight to the heart.

Detoxification of dangerous, bad fat takes place only after the heart has given the fat-laden fluid a powerful push to pump it through the system and the droplets of fat happen to end up in one of the blood vessels of the liver. The liver contains quite a large amount of blood, and so the probability is high that such a meeting will take place sooner rather than later, but before that happens, our heart and our blood vessels are at the mercy of everything that McDonald's and similar fast-food outlets were able to get hold of at the lowest purchase price.

Just as bad fat can have a negative effect, good fat can work wonders. Those who are prepared to spend that little bit extra on cold-pressed (extra virgin) olive oil will be dunking their baguette in a soothing balm for their heart and blood vessels. Many studies have been carried out into the effects of olive oil, and results show that it can protect against arteriosclerosis, cellular stress, Alzheimer's, and eye diseases such as macular degeneration. It also appears to have beneficial effects on inflammatory diseases such as rheumatoid arthritis and help in protecting against certain kinds of cancer. Of particular interest to those fighting fat is that olive oil also has the potential to help get rid of that spare tire. It blocks an enzyme in fatty tissue —known as fatty acid synthase—that likes to create fat out of spare carbohydrates. And we are not the only ones who benefit from the properties of olive oil—the good bacteria in our gut also appreciate a little pampering.

Good-quality olive oil costs a little bit more. However, it tastes neither greasy nor rancid, but rather green and fruity, and it sometimes leaves a peppery feeling in your throat after you swallow it. This is due to the tannins it contains. If this description sounds too abstract, simply try out various oils to find the best, using the various quality seals as a guide.

But merrily drizzling your olive oil into the pan for frying is not such a good idea as heat can cause a lot of damage. Hotplates are great for frying up steaks or eggs, but they are not good for oily fatty acids, which can be chemically altered by heat. Cooking oil or solid fats such as butter or hydrogenated coconut oil should be used for frying. They may be full of the much-frowned-upon saturated fats, but they are much more stable when exposed to heat.

Fine oils are not only sensitive to heat, they also tend to capture free radicals from the air. Free radicals do a lot of damage to our bodies because

they don’t actually like being free, much preferring to bond with other substances. They can latch onto almost anything—blood vessels, facial skin, or nerve cells—causing inflammation of the blood vessels (vasculitis), aging of the skin, or nerve disease. That’s why you should always close the bottle or container of olive oil carefully after use and keep it in the fridge.

The animal fats found in meat, milk, and eggs contain far more arachidonic acid than vegetable fats. Arachidonic acid is converted in our body into neurotransmitters involved in the sensation of pain. Oils such as rapeseed (canola), linseed, or hempseed oil, on the other hand, contain more of the anti-inflammatory substance alpha-linolenic acid, while olive oil contains a substance with a similar effect called oleocanthal. These fats work in a similar way to ibuprofen or aspirin, but in much smaller doses. So, although they are no help if you have an acute headache, using these oils regularly can help those who suffer from inflammatory disease, regular headaches, or menstrual pain. Sometimes, pain levels can be reduced somewhat simply by taking care to eat more vegetable fat than animal fat.

However, olive oil should not be seen as a panacea for all skin and hair conditions. Dermatological studies have shown that pure olive oil can even irritate the skin slightly, and that using olive oil as a hair treatment leaves hair so oily that the amount of washing required to remove the oil negates any possible beneficial effects.

It is easy to overdo it with fats inside our bodies, too. Large amounts—of either good or bad fat—are simply too much for the body to deal with. It’s comparable to smearing too much moisturizer on your face. Nutritional physiologists recommend we get between 25 and a maximum of 30 percent of our daily energy requirement from fat. That works out at an average of 2 to 2½ ounces (55 to 66 grams) of fat a day. Larger, more athletic types may consume a little more; smaller, more sedentary types should try to consume a little less. This means if you eat just one Big Mac, you will have conveniently covered half your daily requirement of fat—the only question is, with what kind of fat? A sweet onion chicken teriyaki sandwich from the fast-food chain Subway contains less than 1/6 of an ounce of fat (only 4.5 grams). How you consume the other 2 ounces (53 grams) is then entirely up to you.

Having examined carbohydrates and fats, there is just one more nutritional building block to consider. It is probably the least familiar:

amino acids. It seems strange to imagine, but both tofu, with its neutral-to-nutty taste, and salty, savory meat are made up of lots of tiny acids. As with carbohydrates, these tiny building blocks are linked in chains. This is what gives them their different taste and a different name—proteins. Digestive enzymes break down these chains in the small intestine and then the gut wall nabs the valuable components. There are twenty of these amino acids and an infinite variety of ways they can be linked to form proteins. We humans use them to build many substances, not least of which is our DNA, the genetic material contained in every new cell we produce every day. The same is true of other living things, both plants and animals. That explains why everything nature produces that we can eat contains protein.

However, maintaining a healthy meat-free diet that does not lead to nutritional deficiencies is more difficult than most people think. Plants construct different proteins than animals, and they often use so little of a given amino acid that the proteins they produce are known as incomplete. When our body tries to use these to make the amino acids it needs, it can continue to build the chain only until one of the amino acids runs out. Half-finished proteins are then simply broken down again, and we excrete the tiny acids in our urine or recycle them in our body. Beans lack the amino acid methionine; rice and wheat (and its derivative meat substitute, seitan) lack lysine; and sweetcorn is, in fact, deficient in two amino acids: lysine and tryptophan. But this does not spell the final triumph of the meat eaters over the meat-avoiders. Vegetarians and vegans simply have to be cleverer in combining their foods.

Beans may be lacking in methionine, but they are packed with lysine. A wheat tortilla with refried beans and a yummy filling will provide all the amino acids the body needs for healthy protein production. Vegetarians who eat cheese and eggs can compensate for incomplete proteins that way. For centuries in many countries around the world, people have intuitively eaten meals made up of foodstuffs that complement each other: rice and beans, pasta with cheese, pita bread and hummus, or peanut butter on toast. In theory, combining does not even have to take place within one meal. It is enough to take in the right combination over the course of a day. (Thinking about these combinations can often inspire even the most uninventive of cooks when they are trying to decide what to make for dinner.) There are plants that do contain all the necessary amino acids in the necessary

quantities. Two of these are soy and quinoa, but others include amaranth, spirulina, buckwheat, and chia seeds. Tofu has a well-deserved reputation as an alternative to meat—with the caveat that increasing numbers of people are developing allergic reactions to it.

Allergies and Intolerances

ONE THEORY ABOUT the origin of allergies begins with the digestive processes in the small intestine. If we fail to break down a protein into its constituent amino acids, tiny bits of it will remain. Under normal circumstances, those tiny particles simply don't make it into our bloodstream and there is no problem. However, hidden power often lies in the most inconspicuous places—in this case, in the lymphatic system. Those tiny particles can enter the lymphatic system, embedded in fat droplets, and once there, they attract the attention of ever-vigilant immune cells. When the immune cells discover a tiny particle of peanut in the lymphatic fluid, for example, they naturally attack it as a foreign body.

The next time the immune cells encounter a peanut particle, they are better prepared to deal with it and can attack it more aggressively. And so it goes on, until we reach the stage where just putting a peanut in our mouth causes our immune cells to whip out the big guns straightaway. The result is increasingly severe allergic reactions, such as extreme swelling of the face and tongue. This explanation applies to allergies caused by foods that are both fatty and rich in protein, such as milk, eggs, and, most commonly, peanuts. There is a simple reason almost no one is allergic to greasy bacon. We are made of meat ourselves, and so we generally have few problems digesting it.

Celiac Disease and Gluten Sensitivity

Allergies that develop in the small intestine are not limited to fats. Allergens such as prawns, pollen, or gluten, for example, are not, in themselves, fat-bombs, and people who eat a fatty diet do not necessarily suffer from more allergies than others. Another theory about how allergies develop is this: the wall of our gut can become temporarily more porous, allowing food remnants to enter the tissue of the gut and the bloodstream.

This is the theory under most scrutiny from researchers who are interested in gluten—a protein found in wheat and related grains.

Grains do not like us to eat them. What plants really want is to reproduce—and then along we come and eat their children. Instead of creating an emotional scene, plants respond by making their seeds slightly poisonous. That sounds much more drastic than it is—neither side is going to lose much sleep over a few guzzled wheat grains. The arrangement means humans and plants both survive well enough. But, the more danger a plant senses, the more poisonous it will make its seeds. Wheat, in particular, is such a worrier because it has only a very short window of opportunity for its seeds to grow and carry on the family line. With such a tight schedule, nothing must be allowed to go wrong. In insects, gluten has the effect of inhibiting an important digestive enzyme. A greedy grasshopper might be put off by a little stomachache after eating too much wheat, and that is to the benefit of both plant and animal.

In humans, gluten can pass into the cells of the gut in a partially undigested state. There, it can slacken the connections between individual cells. This allows wheat proteins to enter areas they have no business being in. That, in turn, raises the alarm in our immune system. One person in a hundred has a genetic intolerance to gluten (celiac disease), but a considerably higher proportion suffer from gluten sensitivity.

In patients with celiac disease, eating wheat can cause serious infections or damage to the villi of the gut wall; it can also damage the nervous system. Celiac disease can cause diarrhea and failure to thrive in children, who may show reduced growth or winter pallor. The tricky thing about celiac disease is that it can appear in more or less pronounced forms. Those with more subtle forms may live with the symptoms for years without realizing it. They may have the occasional stomachache, or their doctor might discover signs of anemia during routine blood tests. Currently, the most effective treatment is a lifelong gluten-free diet.

Gluten sensitivity, by contrast, is not a sentence to a life of gluten avoidance. Those with this condition can eat wheat without risking serious damage to their small intestine, but they should enjoy wheat products in moderation—a little bit like our friend the greedy grasshopper. Many people notice their sensitivity when they swear off gluten for a week or two and see an improvement in their general well-being. Suddenly, their

digestive problems or flatulence clear up, or they have fewer headaches or less painful joints. Some people find that their powers of concentration improve, or that they are less plagued by tiredness or fatigue. Researchers began exploring gluten sensitivity in detail only recently. Currently, the diagnostic picture can be summarized as follows. Symptoms improve when a gluten-free diet is introduced, although tests for celiac disease show negative. The villi are not inflamed or damaged, but eating too much bread still appears to have an unpleasant effect on the immune system.

The gut can also become porous for a short time after a course of antibiotics, after a heavy bout of drinking alcohol, or as a result of stress. Sensitivity to gluten resulting from these temporary causes can sometimes look the same as the symptoms of true gluten intolerance. In such cases, it can be helpful to avoid gluten for a time. A thorough medical examination and the detection of certain molecules on the surface of the blood corpuscles are important for a definitive diagnosis. Alongside the familiar blood groups A, B, AB, and O, there are many other indicators for categorizing human blood, including what doctors call DQ markers. Those who do not belong to group DQ2 or DQ8 are extremely unlikely to have celiac disease.

Lactose Intolerance and Fructose Intolerance

Lactose intolerance is not an allergy or a real intolerance at all, but a deficiency. But it, too, results from a failure to break down certain nutrients completely into their component parts. Lactose is found in milk. It is derived from two sugar molecules that are linked together by chemical bonds. The body requires a digestive enzyme to break that bond, but, unlike other enzymes, this one does not come from the papilla. The cells of the small intestine secrete it themselves on the tips of their tiny little villi. Lactose breaks down when it comes into contact with the enzyme on the gut wall, and the resulting single sugars can then be absorbed. If the enzyme is missing, similar problems arise to those caused by gluten intolerance or gluten sensitivity, including bellyache, diarrhea, and flatulence. Unlike in celiac disease, however, no undigested lactose particles pass through the gut

wall. They simply move on down the line, into the large intestine, where they become food for the gas-producing bacteria there. Consider the resulting flatulence and other unpleasant symptoms as votes of thanks from extremely satisfied, overfed microbes. Although the results can be unpleasant, lactose intolerance is far less harmful to health than undiagnosed celiac disease.

Every human being has the genes needed to digest lactose. In extremely rare cases, problems with lactose digestion can occur from birth. Such newborns are unable to digest their mother's milk, and drinking it causes severe diarrhea. In 75 percent of the world's population, the gene for digesting lactose slowly begins to switch off as they get older. This is not surprising, as by then we are no longer reliant on our mothers' milk, or formula milk, to nourish us. Outside of Western Europe, Australia, and the United States, adults who are tolerant to dairy products are a rarity. Even in our parts of the world, supermarket shelves are increasingly full of lactose-free products. Recent estimates say about 25 percent of people in the United States lose their ability to break down lactose after weaning. The older a person, the greater the probability that she will be unable to break down lactose—although very few sixty-year-olds would dream of blaming their daily glass of milk or that delicious dollop of cream for a bloated stomach or a little bit of diarrhea.

However, lactose intolerance does not mean you must cut out milk products altogether. Most people have enough lactose-splitting enzymes in their gut. It is just that their activity is somewhat reduced—down to about 10 to 15 percent of their initial level, let's say. So if you notice your stomach feels better when you don't drink that glass of milk, you can simply use trial and error to find out just how much your body can deal with, and how much dairy produce it takes to make the problems come back. A nibble of cheese or a splash of milk in your tea or coffee will usually be fine, as will the occasional milk pudding or cream filling in your cake.

A common children's counting rhyme in Germany, comparable to the "eeny, meeny, miny, moe" of the English-speaking world, translates as "Ate cherries, drank water, got tummy ache, went to hospital!" The most common food intolerance in the Western hemisphere is trouble digesting the fruit sugar fructose, with about 40 percent of the population affected.

Fructose intolerance can be the result of a severe hereditary inability to metabolize fruit sugar, which causes patients' digestive systems to react to even the tiniest amounts of the substance. But most people affected by fructose intolerance actually have a condition more accurately described as fructose malabsorption, and they experience problems only when they are exposed to large amounts of the sugar. When fructose is described on food packages as "fruit sugar," consumers often assume it is a healthier, more natural option. This explains why food manufacturers choose to sweeten their products with pure fructose, and consequently why our digestive system is exposed to more of this type of sugar than ever before.

An apple a day would not present a problem to most people who are fructose intolerant if it weren't for the fact that the ketchup on their fries, the sweetening agent in their breakfast yogurt, and the can of soup they heated up for lunch, all contain added fructose. Some types of tomato are specially bred to contain large amounts of this sugar. Furthermore, globalization and air transport mean that we are now exposed to a previously unheard-of overabundance of fruit. Pineapples from the tropics nestle on our supermarket shelves in the middle of winter, next to fresh strawberries from Mexico, and some dried figs from Morocco. So, what we label a food intolerance may in fact be nothing more than the reaction of a healthy body as it tries to adapt within a single generation to a food situation that was completely unknown during the millions of years of our evolution.

The mechanism behind fructose intolerance is different once again from that involved in the digestion of gluten or lactose. The cells of people with hereditary fructose intolerance contain fewer fructose-processing enzymes. That means fructose may gather in their cells, where it can interfere with other processes. Fructose intolerance that appears later in life is thought to be caused by a reduced ability of the gut to absorb fruit sugars. Such patients often have fewer transporters (called GLUT5 transporters) in their gut wall. When they ingest even a small amount of fruit sugar—for example, by eating a pear—their limited transporters are overwhelmed and, as with lactose intolerance, the sugar from the pear ends up feeding the flora of the large intestine. However, some researchers question whether a lack of sufficient transporters really is the cause of this problem, since even those without the condition pass some of the fructose they eat into the large

intestine undigested (especially after eating very large amounts of it). The problems experienced by such people may be due to an imbalance in their gut flora. When they eat a pear, the extra sugar is gobbled up by the gut bacteria squad, which then produces rather unpleasant symptoms. Of course, the more ketchup, canned soup, or sweetened yogurt they have eaten, the worse their troubles will be.

Fructose intolerance can also affect our mood. Sugar helps the body absorb many other nutrients into the bloodstream. The amino acid tryptophan likes to latch on to fructose during digestion, for example. When there is so much fructose in our gut that most of it cannot be absorbed into the blood and we lose that sugar, we also lose the tryptophan attached to it. Tryptophan, for its part, is needed by the body to produce serotonin—a neurotransmitter that gained fame as the happiness hormone after it was discovered that a lack of it can cause depression. Thus, a long-unrecognized fructose intolerance can lead to depressive disorders. General practitioners and family doctors are only now beginning to include this knowledge in their diagnostic toolkit.

This raises the question whether a diet that includes too much fructose can also affect our mood, even in the absence of an intolerance. For more than 50 percent of people, eating 2 ounces (50 grams) of fructose or more per day (equivalent to five pears, eight bananas, or about six apples) will overtax their natural transporters. Eating more than that can lead to health problems such as diarrhea, stomachaches, and flatulence, and, over longer periods, to depressive disorders. The fructose intake of the average American is currently close to 3 ounces (80 grams) a day. Our parents' generation, consuming just honey on their toast, far fewer processed foods, and a normal amount of fruit, took in no more than ½ to 1 ounce (only around 16 to 24 grams) a day.

Serotonin not only puts us in a good mood, it is also responsible for making us feel pleasantly full after a meal. Snack attacks or constant grazing on snacks may be a side effect of fructose intolerance if they are accompanied by other symptoms, such as stomachaches. This is also an interesting hint for all diet-conscious salad eaters, since many salad dressings found on our supermarket shelves or at fast-food outlets now contain fructose-glucose syrup (often known as high-fructose corn syrup). Studies have shown that this syrup can suppress leptin, the hormone that

makes us feel full, even in people who are not fructose intolerant. A salad containing the same amount of calories but with a homemade vinaigrette or yogurt dressing will keep you feeling full for longer.

Like everything else in the world, food production is constantly changing. Sometimes those changes are good for us and sometimes they are bad. Curing was once the state-of-the-art way of ensuring people were not poisoned by eating rotten meat. For centuries, it was common practice to cure meats and sausages with large quantities of nitrite salts. This gives them a pinkish red, fresh color, and explains why products such as ham, salami, tinned pork, or gammon do not turn the same brown-gray color in the frying pan as an unprocessed chop or steak.

Use of nitrites for food preservation has been highly regulated since the 1980s, due to concerns about possible negative effects on human health. In the United States, sausage and cold meat products must contain no more than 156 parts per million of nitrite salt, approximately one-fifth of the level allowed twenty-five years ago. Rates of stomach cancer have fallen considerably since these regulations were introduced. This shows that what had once been a very sensible meat-preserving technique was in drastic need of correction. Today, canny butchers mix large amounts of vitamin C with small amounts of nitrite to cure their meats safely.

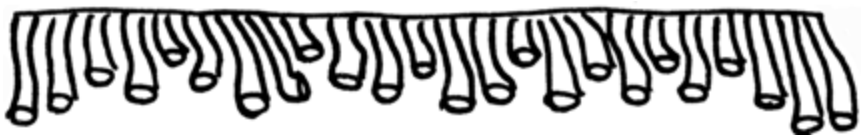
A similar modern reassessment of ancient practices may be in order in the case of wheat, milk, and fructose. It is good to include these foodstuffs in our diet, since they contain valuable nutrients, but it may be time to reassess the quantities we consume. While our hunter-gatherer ancestors ate up to five hundred different local roots, herbs, and other plants in a year, a typical modern diet includes seventeen different agricultural plant crops at most. It is not surprising that our gut has a few problems with a dietary change of that scale.

Digestive issues divide society into two groups: those who worry about their health and pay great attention to their nutrition, and those who get annoyed by the fact that they can no longer invite a group of friends round for a meal without having to go shopping at the pharmacy. Both groups are right. Many people err on the side of caution after hearing from their doctor about a food intolerance and then noticing that they do feel better if they avoid certain foods. They might decide to cut out fruit, wheat, or dairy products, and then often act as if they were poisonous. In fact, most people

react to excessive amounts of these foodstuffs without being genetically intolerant to them. Most have enough enzymes to process a small portion of creamy sauce, the occasional pretzel, or a fruit pudding.

However, this does not mean that real intolerances should be ignored. We do not need to swallow every new development in our food culture blindly. Wheat products for breakfast, lunch, and dinner, fructose in practically all processed foods, or milk products long after weaning—it is not surprising that our bodies sometimes rebel. Symptoms like regular stomachaches, repeated bouts of diarrhea, or severe fatigue do not occur for no reason, and nobody should be expected to just accept them as “one of those things.” Even if your doctor has ruled out celiac disease or hereditary fructose intolerance, nobody can deny you the right to avoid certain foods if you notice that doing so improves your general well-being.

Apart from this general overconsumption, antibiotics, high stress levels, or gastrointestinal infections, for example, can also trigger temporary sensitivities to certain foods. When the body has returned to a healthy equilibrium, even a sensitive gut can usually sort itself out. Then there is no need to impose a lifelong ban on certain products, but simply to make sure you consume them in quantities your system can easily cope with.

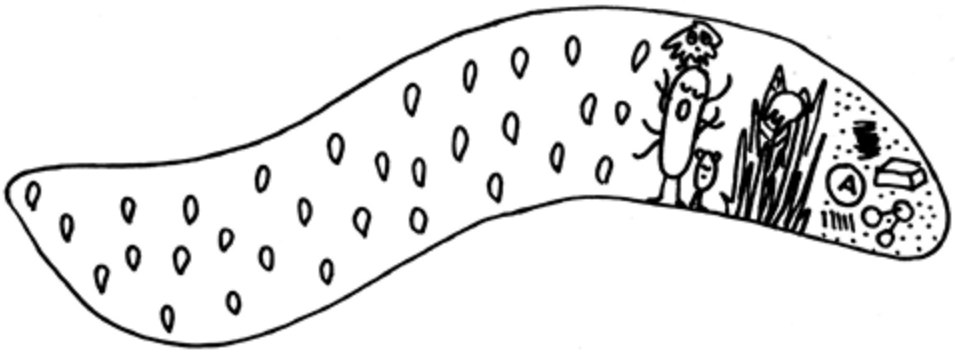


A FEW FACTS ABOUT FECES

GENTLE READER, it is now time to get down to the nitty-gritty. So, hitch up your suspenders, push your glasses up the bridge of your nose, and take a good gulp of your tea. While maintaining a safe distance, we must now take a closer look at the mysteries of number twos!

COMPONENTS

Many people believe feces are made up mainly of what they have eaten. That is not the case.



Feces are three-quarters water. We lose around 3½ ounces (100 milliliters) of fluid a day. During a passage through our digestive system, some 10 US quarts (9.8 liters) are reabsorbed. What we deliver into the toilet bowl is the result of an absolute maximum level of efficiency. Whatever fluid is left in the feces belongs there. This optimum water content makes our feces soft enough to ensure our metabolic waste products can be transported out of our bodies safely.

A third of the solid components are bacteria. They are gut flora that have ended their careers in the digestive business and are ready to retire from the workplace.

Another third is made up of indigestible vegetable fiber. The more fruit and vegetables you eat, the more feces you excrete per bowel movement. Increasing the proportion of that food group in the diet can raise the weight of a bowel movement from the average 3½ to 7 ounces (100 to 200 grams) to as much as 17 or 18 ounces (500 grams) per day.

The remaining third is a mixed bag. It is made up of substances that the body wants to get rid of—such as the remains of medicines, food coloring, or cholesterol.

COLOR

The natural color of human feces ranges from brown to yellowish-brown—even when we have not eaten anything of this color. The same is true of our urine—it always tends toward yellow. This is due to a very important product that we manufacture fresh every day: blood. Our bodies create 2.4 million new blood corpuscles a day. But the same number are broken down every day, too. In that process, the red pigment they contain is first turned green, then yellow. You can see the same process in the various stages of a bruise on your skin. A small portion of this yellow pigment is excreted in your urine.

Most of it, though, passes through the liver and into the gut. There, bacteria change its color once again—this time turning it brown. Examining the color of feces can provide a useful insight into the goings-on of our gut.

LIGHT BROWN TO YELLOW: This color can be the result of the harmless disorder called Gilbert's syndrome (or Gilbert-Meulengracht syndrome). In this condition, one of the enzymes involved in the breakdown of blood works at only 30 percent of its normal efficiency. This means less pigment finds its way into the gut. Affecting around 8 percent of the world's population, Gilbert's syndrome is relatively common. This enzyme defect is not harmful, causing barely any problems for those who have it. The only side effect is a reduced tolerance for acetaminophen, which should be avoided by those with Gilbert's syndrome.

Another possible cause of yellowish feces is problems with the bacteria in the gut. If they are not working as they should, the familiar brown

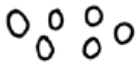
pigment will not be produced. Antibiotics or diarrhea can cause such an alteration in fecal color.

LIGHT BROWN TO GRAY: If the connection between the liver and the gut is blocked by a kink in the tubes or by pressure (usually behind the gall bladder), no blood pigment can make it into the feces. Blocked connections are never a good thing, and those who notice a gray tint to their feces should consult their doctor.

BLACK OR RED: Congealed blood is black and fresh blood is red. In this case, the color is not due to the pigment that can be turned brown by bacteria, but to the presence of entire blood corpuscles. For those with hemorrhoids, a small amount of bright red blood in the stool is no reason to worry. However, anything darker in color than fresh, bright red blood should be checked by a doctor—unless you have been eating large amounts of beetroot.

CONSISTENCY

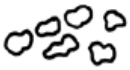
The Bristol stool scale was first published in 1997, so it is not very old if you consider the millions of years that feces have existed. The scale classifies the consistency of feces into seven groups. A chart like this can be a useful tool, since most people are reluctant to talk about the appearance of their bowel movements. That’s perfectly natural. There are some aspects of private life we prefer not to rub other people’s noses in! But such a reticence to talk about what we find in the toilet bowl means that people with unhealthy looking feces are often unaware of it. They think everybody’s business looks like their own. A healthy digestive system, producing feces with the optimum water content, will produce types 3 or 4. The other types are less than ideal. If they do appear, a good doctor should be able to find out whether your loose stool or constipation is the result of a food intolerance, for example. The chart was developed by Dr. Ken Heaton at the University of Bristol in the United Kingdom.

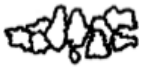
 TYPE 1 Separate hard lumps, like nuts (hard to pass)

TYPE 2 Sausage-shaped, but lumpy

TYPE 3 Like a sausage but with cracks on its surface

TYPE 4 Like a sausage or snake, smooth and soft (author's note: like toothpaste)

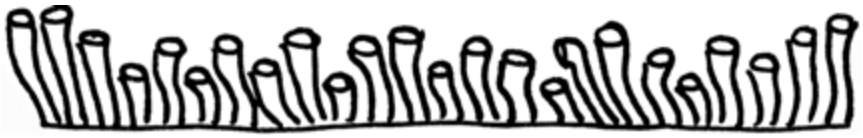
 TYPE 5 Soft blobs with clear-cut edges (passed easily)

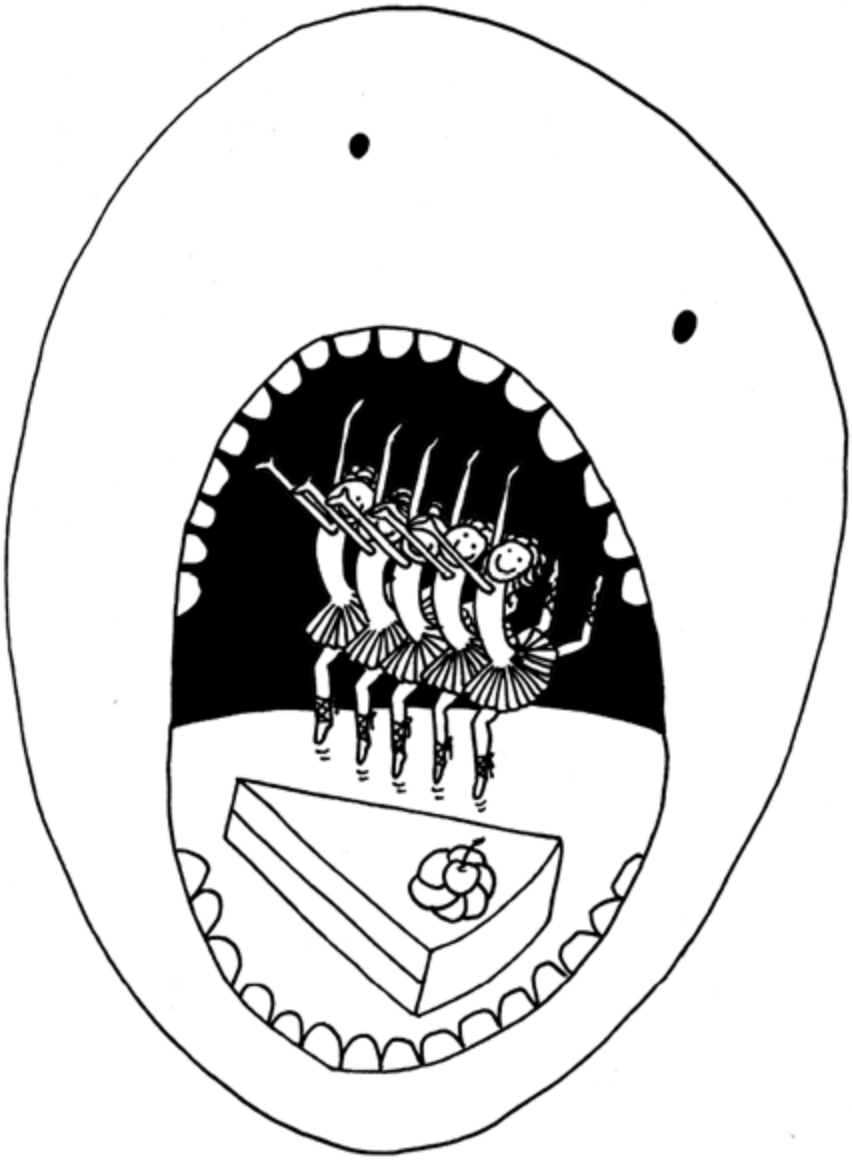
 TYPE 6 Fluffy pieces with ragged edges, a mushy stool

TYPE 7 Watery, no solid pieces, entirely liquid

The type a person's feces belong to can be an indication of how long indigestible particles take to pass through their gut. According to this, in Type 1 digestive remains take around one hundred hours to pass through the system (constipation). In Type 7, they pass through in just ten hours (diarrhea). Type 4 is considered the ideal, because it has the optimum ratio between fluid and solid content. Those who find types 3 or 4 in the toilet bowl may also want to observe how quickly their feces sink in water. Ideally, they should not plummet straight to the bottom, as this would indicate the possibility that they still contain nutrients that have not been digested properly. Feces that sink slowly contain bubbles of gas that keep them afloat in water. These gas bubbles are produced by gut bacteria that mostly perform useful services. So this is a good sign, as long as it is not accompanied by flatulence.

THESE HAVE BEEN a few selected facts about feces, gentle reader. You can now loosen your suspenders and let your glasses slide back down your nose to where they are most comfortable. Here endeth the first chapter of the story of the gut and its goings-on. We now turn to an electrifying topic: the nerves.





(PART TWO)

THE NERVOUS SYSTEM OF THE GUT

THERE ARE PLACES where the unconscious and the conscious meet. When you are sitting at home, eating your lunch, you may be unaware that your next-door neighbor is just a short distance away, beyond the dividing wall, chomping away on his lunch, too. You might hear the faint creak of his floorboards and suddenly, your awareness reaches out beyond your own four walls. Similarly, there are areas of our own body we are simply unaware of. You don't feel your organs working away all day long. When you eat a piece of cake, you taste it while it is still in your mouth, and you are also conscious of the beginning of its journey as it passes down your throat after you swallow it. But then, as if by magic, the cake is gone! From then on, what we eat disappears into the realm of what scientists call smooth muscle.

Smooth muscle is not under our conscious control. Under the microscope, it looks very different from the tissue of the muscles we can control consciously, such as the biceps. We can flex and relax the muscles in our upper arms at will. Such muscles are made up of the tiniest little fibers, lined up so neatly they look as if they were drawn using a ruler.

The microscopic structure of smooth muscle resembles an organic network, and it moves in mellifluous waves. Our blood vessels are surrounded by smooth muscle tissue, which explains why we blush when we are embarrassed. Smooth muscle tissue slackens in response to emotions such as embarrassment, causing the blood capillaries in the skin of the face to dilate. In many people, stress has the opposite effect, causing the muscles surrounding the blood vessels to contract, restricting the flow of blood. This can lead to high blood pressure.

The gut is cosseted by no fewer than three coats of smooth muscle tissue. This makes it incredibly supple and able to execute different choreographies in different places. The choreographer directing these muscles is the gut's own (enteric) nervous system. The enteric nervous system controls all processes that take place in the digestive tract, and it is extra-ordinarily autonomous. If the connection between the enteric nervous system and the brain is severed, the digestive tract carries blithely on as if nothing has happened. This property is unique to the enteric nervous system and is found nowhere else in the human body—without directions from our brain, our legs would be lame and our lungs would no longer be able to breathe. It

is a shame that we are oblivious to the workings of these independent-minded nerve fibers. Burping or breaking wind might sound a bit gross, but the movements involved are as delicate and complex as those of a ballerina.

How Our Organs Transport Food

ALLOW ME TO take you on a journey. Let us accompany that piece of cake on its travels in the realm of smooth muscle.

Eyes

Particles of light bouncing off the piece of cake hit the optic nerves at the back of the eyes, generating a nerve impulse. This first impression travels right through the brain to the visual cortex at the back, just below where a high ponytail would be. There, the brain interprets the nerve impulses to form an image. It is not until that happens that we really see the piece of cake. This delicious news is then passed on to the systems that control salivation, with mouth-watering results. Similarly, the mere sight of a yummy treat also causes the stomach to produce some digestive juices in anticipation.

Nose

If you stick your finger up your nose, you will notice that the cavity continues upward far beyond the reach of your finger. This is where the olfactory nerves are, which are responsible for smelling. They are coated in a protective layer of mucus, so anything we smell must first be dissolved in that slimy substance if it is to get through to the nerves.

Olfactory nerves are specialists. There are specific receptors for a large range of individual smells. Some spend years hanging around up your nose, waiting for their chance to shine. When that single, long-awaited lily-of-the-valley scent molecule finally attaches itself, the receptor proudly calls out “lily-of-the-valley!” to the brain. Then it might be idle again for the

next couple of years. (Incidentally, although we are equipped with a large number of olfactory cells, dogs have inconceivably more.)

For us to smell it, molecules from the piece of cake first have to drift into the air, to be sucked in through our nostrils as we breathe. They may be aromatic molecules of vanilla, minute plastic molecules from cheap party forks, or evaporating alcohol fragrances from the cake's rum filling. Our olfactory organ is a royal taster with a thorough knowledge of chemistry. The closer we bring the cake-laden fork to our cake-hole, the more detached cake molecules stream into our nose. If we detect tiny traces of alcohol as the cake covers the last small gap between our fork and our mouth, we may back our arm up in suspicion to allow our eyes to inspect the cake again, just to check whether it is supposed to contain alcohol or whether the fruit in it has started to rot. With all checks passed, it's mouth open, fork in, and let the ballet begin.

Mouth

The mouth is a place of superlatives. The most powerful muscles in our body are the jaw muscles; the body's most flexible striated (not smooth) muscle is the tongue. Working together, they are not only incredible crunchers, they are also nimble manipulators. Another candidate for the record books is tooth enamel. Tooth enamel is the hardest substance produced by the human body. And it needs to be, since our jaws can exert a pressure of up to 180 pounds (80 kilos) on each of our molars—or approximately the weight of a grown man! When we encounter something hard in our food, we pound it with almost the equivalent force of an entire football team jumping up and down on it before we swallow it. All that power is not necessary to deal with a piece of cake—just a few girls in tutus and ballet slippers will suffice.

The tongue plays an important part in mastication. It acts like a football coach, gathering any bits of cake that may be hiding from the chewing action and guiding them back into the game. When the mouthful of cake is sufficiently mushy, it is ready for swallowing. The tongue rounds up about half an ounce (20 milliliters) of cake mush and presses it against the palate,

the stage curtain of the esophagus. It works like a light switch: when the tongue presses against it, the swallowing reflex starts automatically. We close our mouth, since breathing must stop for swallowing to take place. The ball of cake mush—known medically as the bolus—now makes its way toward the pharyngeal area, and it's time for the dancers to enter the stage and the show to start.

Pharynx

The velum (or soft palate) and the superior pharyngeal constrictor muscle are the two formations responsible for officially closing the connections to the nose. This movement is so powerful that it can be heard down the corridor and round the corner—that popping sound in the ear that often accompanies a powerful swallow. The vocal cords are silenced and have to be closed. The epiglottis rises majestically, like an orchestra conductor (you can feel it when you place a hand on your neck), the entire base of the mouth is lowered, and a powerful wave pushes the bit of cake into the esophagus, amid tumultuous applause from the salivary system.

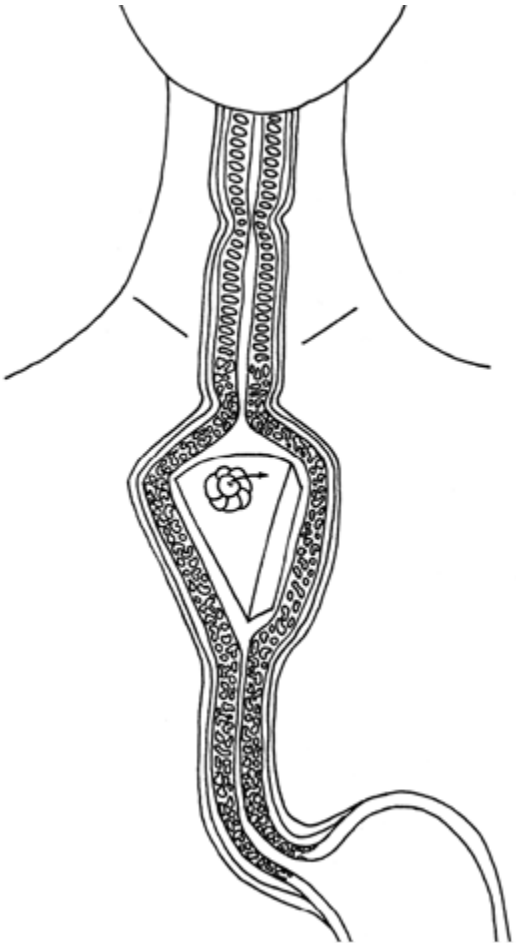
Esophagus

The cake bolus takes five to ten seconds to reach this stage. When we swallow, our esophagus executes a kind of stadium-style wave. On the arrival of the bolus, the esophagus widens to let it pass, closing again behind it. This prevents anything from slipping back up the wrong way.

This process is so automatic that it even works when the owner of the esophagus is standing on her head. Our piece of cake meanders in this way—oblivious to gravity—gracefully through the upper body. Break dancers would call this move The Snake or The Worm; doctors prefer to call it propulsive peristalsis. The top third of the esophagus is surrounded by striated muscle—that is why we are still aware of the cake passing through that part of the gullet. The unconscious inner world begins at the level of

that small hollow you can feel at the top of your breastbone. From there on, the esophagus is made of smooth muscle.

The esophagus is sealed at the bottom end by a ring-shaped sphincter muscle. Taking its cue from the peristaltic motion above, that muscle relaxes for eight frolicsome seconds. This opens the way, allowing the piece of cake to plop unhindered into the stomach. The muscle then closes again, and normal breathing service resumes up in the pharynx.



The journey from mouth to stomach is the first act of the performance. It requires maximum concentration and good teamwork. The conscious peripheral nervous system and the unconscious autonomous nervous system must work together in perfect harmony. This cooperation must be well rehearsed. We begin practicing swallowing as unborn babies in the womb. We swallow up to one pint (half a liter) of amniotic fluid a day during this test phase. If something goes wrong at this stage, no harm is done. Since we

are completely surrounded by liquid, and our lungs are full of it anyway, we are unable to choke in the normal sense.

As adults, we swallow somewhere between six hundred and two thousand times a day. And each act of swallowing involves more than twenty pairs of muscles. Despite this frequency and complexity, things rarely go wrong. In old age, we are more prone to choking. The muscles that coordinate the process may no longer work quite so precisely. The superior pharyngeal constrictor muscle might not be quite the strict timekeeper it was in its youth, or the epiglottal conductor may need the aid of a stick to climb up to the podium. Pounding someone on the back when they are choking is a well-meant gesture, but it does little more than startle the aging pharyngeal team unnecessarily. A better strategy is to seek out a speech therapist to help you whip your swallowing squad into good shape before choking attacks become too frequent.

Stomach

The stomach is much more of a mover than many people think. Shortly before our piece of cake plops in, it relaxes to accommodate it—and it can keep relaxing and stretching for as long as food keeps arriving. It will make room for as much as we can guzzle. Two pounds (one kilo) of cake about the size of a carton of milk will easily fit into this stretchable swing hammock of a stomach. Emotions like fear or stress can reduce the ability of the smooth muscle to stretch, making us feel full—or even nauseous—after eating just a small portion of food.

Once the cake arrives, the walls of the stomach speed up their movements, just like the legs of a person accelerating into a run, then—bam!—the food gets a big push. Describing an elegant arc, it is lobbed against the stomach wall, where it bounces off and plops back down. Medics call this process retropulsion. Older brothers and sisters call it “let’s see how far I can throw you.” This acceleration, push, and plop process is what causes the gurgling sound you can hear if you press your ear against the top of someone’s belly (in the little triangle where the ribs meet). When the stomach starts merrily swinging to and fro, the rest of the digestive tract

is galvanized into action as well. This leads the gut to move its contents on down the line, making room for the next batch. That's why we often feel the urge to seek out the toilet soon after enjoying a large meal.

A piece of cake can really get things going in the belly region. The stomach will churn it for about two hours, grinding the mouthfuls into tiny particles, most of them less than one-twelfth of an inch (about 2 millimeters) in size. Scraps of that size are no longer lobbed against the stomach wall, but slip through a little hole at the end of the stomach. This hole is the next sphincter—the doorman who guards the stomach's exit and the entrance to the small intestine.

Simple carbohydrates such as sponge cake, rice, or pasta make it through to the small intestine pretty quickly. There, they are digested and rapidly cause an increase in the levels of sugar in our blood. The doorman detains proteins and fats in the stomach for considerably longer. A piece of steak may easily be churned about for six hours before all of it has disappeared into the small intestine. This explains why we often fancy a sweet dessert after eating meat or fatty, fried foods. Our blood sugar levels are impatient and want to rise quickly, and dessert provides a quick blood sugar fix. Meals rich in carbohydrates may perk us up more quickly, but they do not keep us feeling full for as long as meaty or fatty meals.

Small Intestine

When the mini-morsels reach the small intestine, the real process of digestion begins. As it passes through this tube, the motley cake mush will almost completely disappear into its walls—a bit like Harry Potter on Platform 9¾. The small intestine pluckily pounces on the piece of cake. It squeezes it, hashes it up from all sides, wiggles its villi in what we might now call the cake chyme, and when it is thoroughly mixed, moves it on down the digestive line. Under the microscope we can see that even the microvilli help it along! They move up and down like tiny trampling feet. Everything is in motion.

Whatever our small intestine does, it always obeys one basic rule: onward, ever onward! This is achieved by the peristaltic reflex. The man

who first discovered this mechanism did so by isolating a piece of gut and blowing air into it through a small tube—and the friendly gut blew right back. This is why many doctors recommend a high-fiber diet to encourage digestion: indigestible fiber presses against the gut wall, which becomes intrigued and presses back. These gut gymnastics speed up the passage of food through the system and make sure the gut remains supple.

If our cake chyme were to listen carefully, it might hear a “heave!” The wall of the small intestine contains a particularly large number of pacemaker cells, which emit tiny bioelectric pulses. For the muscles of the gut, that is as if someone were to shout “heave!” and then again “heave!” In this way, the muscle is prevented from drifting off course, and it “heaves” back into place like a clubber on the dance floor responding to the beat. This keeps the piece of cake, or what’s left of it, moving unerringly onward.

The small intestine is the hardest-working part of our digestive tract, and it is very diligent about doing its job. There is only one unequivocal exceptional case when it does not see a digestive project through to the end: when we throw up. The small intestine is quite pragmatic when we need to vomit. It does not invest work in something that will not do us any good. It simply sends such stuff straight back by return mail.

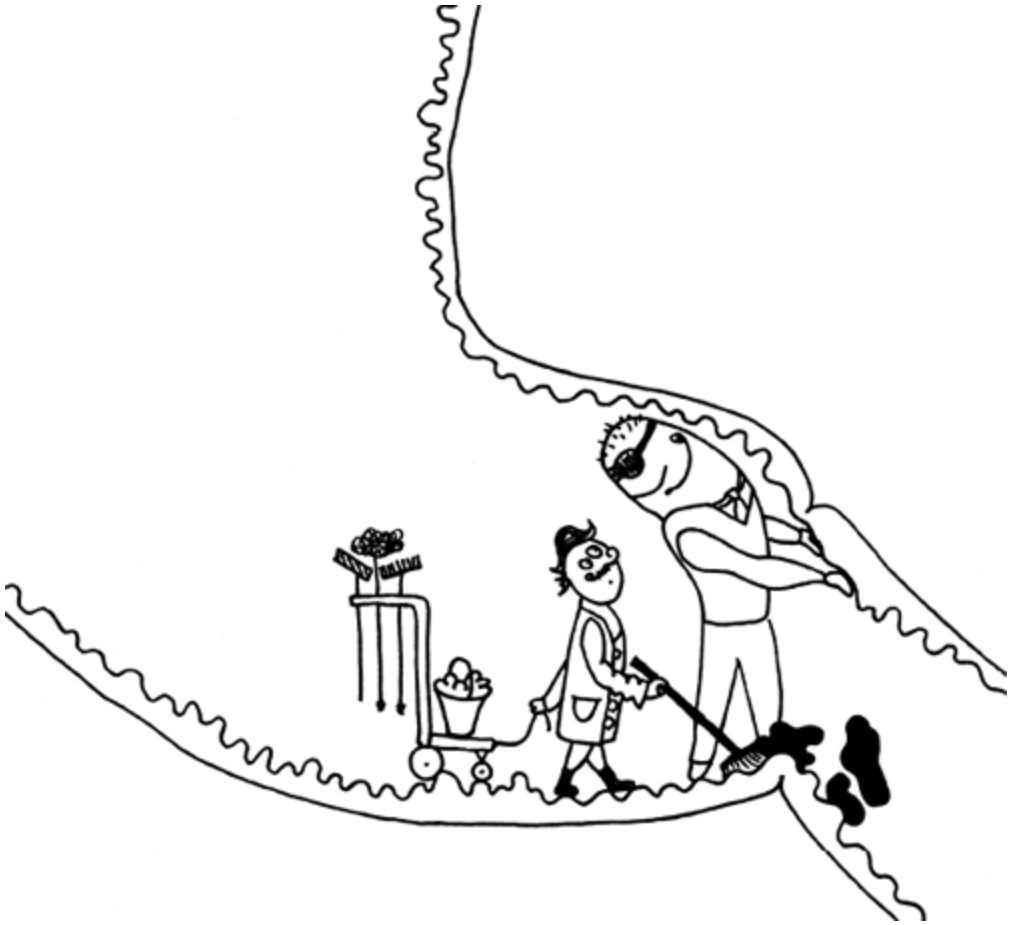
Apart from a few remnants, our piece of cake has now disappeared entirely into the bloodstream. We could now follow those stragglers as they pass into the large intestine, but then we would miss a mysterious and oft-misunderstood creature that we can hear but not see. So let’s stay a little while longer and get acquainted with it.

After digestion, only a few rough leftovers remain in the stomach and small intestine—an unchewed kernel of corn, tablets coated to stop them dissolving in gastric juices, surviving bacteria from the food we have eaten, or a piece of chewing gum swallowed by mistake, for example. Now, the small intestine is a stickler for cleanliness. It is one of those types who clean up the kitchen right after a meal. If you were to pay your small intestine a visit just two hours after it has finished digesting something, you would find everything spick and span, with barely a whiff of what went on there a short time ago.

An hour after the small intestine has digested something, it begins the cleanup process. The scientific name for this process is “migrating motor complex.” When it kicks in, the stomach doorman is kind enough to open

the gates again to allow these leftovers to be herded into the small intestine. It then moves them along with a wave powerful enough to sweep everything along with it. When observed with a camera, this looks so cute that even sober-minded scientists can't help but nickname the migrating motor complex the little "housekeeper."

Everyone has heard their little housekeeper at work. It is the rumbling belly, which, contrary to popular belief, does not come mainly from the stomach, but from the small intestine. Our bellies don't rumble when we're hungry, but when there is a long enough break between meals to finally get some cleaning done! When the stomach and the small intestine are both empty, the coast is clear for the housekeeper to do its work. If the stomach is involved in the lengthy process of grinding down a steak, the housekeeper just has to be patient. Only after six hours of churning in the stomach and around five hours of digesting in the small intestine is the steak safely gone and the housekeeper can start clearing up. We don't necessarily always hear the housekeeper at work. It depends on how much air has found its way into the stomach and the small intestine. If we eat something before the cleanup is finished, the housekeeper immediately stops working and returns to waiting mode. Food needs to be digested in peace and not swept ahead too soon in a cleaning frenzy. Constant snacking means there is no time for cleaning. This is part of the reason some nutritional scientists recommend we leave five hours between meals. There is no scientific evidence proving that the interval must be precisely five hours. Those who chew their food thoroughly create less work for their housekeeper and can listen to their belly when it tells them it's time to eat again.



Large Intestine

At the end of the small intestine is a structure known as Bauhin's valve. It separates the small from the large intestine, which is good because the two neighbors have very different ideas about work ethics. The large intestine is a much more leisurely type. Its motto is not really "onward, ever onward." It is not averse to shifting what remains of our food backward as well as forward if that's what feels right at the time. It has no busy little housekeeper. The large intestine is the tranquil home of our gut flora, which deal with anything that gets swept into the large intestine undigested.

The large intestine works at a more leisurely pace because it has to consider several different players. Our brain is picky about when it wants us

to go to the toilet, the bacteria in our gut want ample time to deal with undigested food, and the rest of our body very much wants to get back the fluids it lent to the digestive system.

What makes it as far as the large intestine no longer resembles a piece of cake—nor should it. The unabsorbed remains of the cake may include a few fruit fibers from the cherry on the top, and the rest is made up of digestive juices, which are reabsorbed here. When we are anxious, our brain jockeys the large intestine along, leaving it without sufficient time to reabsorb all that fluid. The result is diarrhea.

Although the large intestine (like the small intestine) is a smooth tube, it is always shown in diagrams looking like a lumpy string of beads. Why is that? In fact, that is just what the large intestine looks like when the abdomen is opened up. The simple reason for this is that it is engaged in a slow-motion dance. Just like the small intestine, it bulges as it processes the food it receives, so as to hold it where it needs it to be. However, it tends to remain in one position for a long time without moving—something like those street mimes who stand in one statuesque pose until someone comes along and puts a coin in their hat. Every now and then, it relaxes and then forms bulges in other places. Then it remains in that configuration for a while. Anatomy books depict it in this way—like a child who blinks when the class photo is taken to appear in the yearbook looking dopey forevermore.

Two or three times a day, the large intestine stirs from its slumbers and gives an enthusiastic shove to the concentrated food mush to push it forward. Those who provide their large intestine with sufficient bulk may even have to go to the toilet two or three times a day. For most people, the content of their large intestine is enough for one bowel movement a day. But, statistically speaking, three times a day is still a healthy frequency. Women’s large intestines are generally slightly more lethargic than men’s. Medical researchers have not yet discovered why this is so, but the greatest likelihood is that it has a hormonal cause.

The cake’s journey from fork to toilet takes one day on average. Faster guts accomplish this journey in eight hours; for slower digesters, it can take three and a half days. Due to all the mixing they undergo, some cake particles may linger in the chill-out space of the large intestine for twelve hours, while others might lounge around for up to forty-two hours.

Leisurely digesters should not worry as long as the consistency of their bowel movements is fine and they have no other complaints. On the contrary, one Dutch study showed that those who belong to the once a day or less faction and those who have occasional constipation are less likely to contract certain rectal diseases. This is consistent with the motto of the large intestine, “Slow and steady wins the race.”

Reflux

THE STOMACH CAN sometimes stumble. Its smooth muscle tissue can trip up just like the striated muscles of the legs. When that stumble causes a substance like gastric acid to reach places that are not designed to deal with it, it hurts. Reflux is the regurgitation of gastric acid and digestive enzymes into the pharyngeal area; in the case of heartburn, those juices travel no farther than the end of the esophagus, causing a burning sensation in the chest.

Reflux has the same cause as stumbling: it's all down to the nerves. They control our muscles. If the nerves in our eyes fail to detect a doorstep in time, our legs receive incorrect information and carry on walking as if there were no obstacle in the way—and we stumble. When the nerves of our digestive system receive incorrect information, they fail to keep our gastric juices where they belong and allow them to start moving in the wrong direction.

The junction between the esophagus and the stomach is an area that is particularly susceptible to such stumbles. Despite safety measures that include a narrow esophagus, a steadied position in the diaphragm, and the curve at the entrance to the stomach, things sometimes still go wrong. Around a quarter of people in Europe regularly experience such problems. This is not just another modern fad: nomadic people, whose way of life has not changed for hundreds of years, have similar rates of heartburn and reflux to Europeans, although rates are thought to be on the rise in the United States.

The crux of the matter is that two different nervous systems have to work together in the esophagus and stomach area—the nervous system of the brain and that of the gut. For example, the sphincter muscle between the esophagus and the stomach is under the control of nerves from the brain. The brain also influences gastric acid production. The nerves of the digestive tract ensure that the esophagus moves things downward in a harmonious stadium-style wave, keeping it clean with the thousand-or-so times we swallow saliva over the course of a day.

Practical tips to help with heartburn and reflux are based on trying to get those two nervous systems back on the right path. Chewing gum or sipping tea can help the digestive tract because small, repeated swallows help nudge the nerves in the right direction—down toward the stomach, not back up. Relaxation techniques can help persuade the brain not to send out such hectic instructions via the nerves. In a best-case scenario, that should result in constant closure of the sphincter, leading to less acid production.

Cigarette smoke stimulates areas of the brain that are also activated by eating. This may lead to a sense of satisfaction, but it also tricks the brain into producing more gastric acid for no practical reason, as well as causing the sphincter between the esophagus and the stomach to relax. This is why giving up smoking often helps reduce reflux and heartburn complaints.

Pregnancy hormones can cause similar disarray. Their intended function is to keep the womb relaxed and cozy for the unborn baby, but they also have a similar effect on the sphincter of the esophagus. The result is a leaky connection to the stomach, which, combined with the pressure of the bulging belly from below, causes acid to rise. Contraceptives containing female hormones can cause reflux as a side effect.

Cigarette smoke or pregnancy hormones—our nerves are not like fully insulated electric cables. They are embedded organically in our tissues and react to the substances around them. That’s why many doctors recommend avoiding foodstuffs that can reduce the strength of the sealing sphincter: chocolate, hot spices, alcohol, sugary sweets, coffee, and so on.

All these substances influence our nerves, but they do not necessarily cause an acid stomach stumble in everybody. The results of American studies indicate each individual should use trial and error to find out which foods affect their nerves, rather than unnecessarily cutting out everything that might be the culprit.

There is an interesting connection discovered by means of a drug that was never approved because of its side effects. This substance blocks nerves at a location where glutamate normally binds with them. Most people are familiar with glutamate as a flavor enhancer, but it is also released by our nerves. In the nerves of the tongue, glutamate causes an intensification of taste signals. This can create confusion in the stomach, since the nerves do not know whether the glutamate originates from their colleagues elsewhere in the body or from the local Chinese takeaway. The

trial-and-error test here would involve avoiding food rich in glutamate for a while. To do this, you will have to take your reading glasses to the supermarket to check those lists of ingredients in tiny print on food labels. Often, glutamate hides behind more complicated formulations such as monosodium glutamate or something similar. If avoiding it results in an improvement—fine. If not, at least you will have eaten more healthily for a while.

Those whose stomach stumbles less than once a week can turn to simple remedies for relief, such as antacids from the pharmacy or household cures like raw potato juice. Neutralizing stomach acid should not be used as a long-term strategy, however. Stomach acid is useful for combating the harmful effects of allergens and bacteria from our food, and is instrumental in digesting proteins. What is more, some antacid medications contain aluminum, which is a very alien substance for our body to deal with. So, overuse of antacids should be avoided. Always read and follow the instructions on the leaflet.

Reliance on antacids for four weeks or more should be seen as a warning sign. Anyone who ignores such warnings will soon feel the wrath of a disgruntled stomach that wants its acid back—to make up for the effects of the medication for one thing, but also to return to its natural acidic state. Antacids are never a long-term solution for reflux and certainly not for other acidic phenomena, such as gastritis, which is the medical name for an inflammation of the lining of the stomach.

When symptoms continue despite the use of antacids, doctors must get creative to find out why. If blood tests and a thorough physical examination yield no abnormal results, a doctor may prescribe a drug called a proton pump inhibitor, or PPI. PPIs inhibit the production of acid and its secretion into the stomach. Short-term use of a PPI may leave the stomach lacking a little acid, but for those who suffer from heartburn or reflux, they provide a short respite for the stomach and the esophagus so that they can recover from the effects of such acid attacks.

If attacks strike mainly at night, it is a good idea to try propping the upper body up to an angle of 30 degrees. This can involve complex pillow constructions and the use of a protractor at bedtime, but specially manufactured pillows are also available from specialist suppliers. Incidentally, a 30-degree upper body inclination is also good for the

cardiovascular system. My old physiology professor never tired of telling us this, and, given that his specialty is cardiovascular research, I am more than inclined to believe him. But it also means I now can't help imagining him propped up in bed every time someone mentions his name.

Patients *should* lose sleep over such serious warning signs as difficulty swallowing, weight loss, swelling, or any sign of blood. When such symptoms appear, it is high time for an exploratory expedition into the stomach with a camera—no matter how unpleasant an experience that can be. The real danger with reflux comes not, in fact, from burning acid, but from bile reaching the esophagus from the small intestine via the stomach. Bile does not cause a burning sensation, but it has much more insidious effects than acid. Luckily, for most people who suffer from reflux, there is very little bile involved.

The presence of bile can seriously confuse the cells of the esophagus. Suddenly, they are no longer sure where they are, thinking, "Am I really an esophagus cell? I keep sensing bile! Perhaps I've really been a small intestine cell all these years without realizing it... Silly me!" Anxious to do the right thing, they change from esophagus cells into gastrointestinal cells. That can cause problems. Mutating cells can make mistakes in their own programing and no longer grow in a controlled way like other cells. However, this has serious repercussions for only a small percentage of people who suffer from stomach stumbles.

In the vast majority of cases, reflux and heartburn are stumbles that are unpleasant but not dangerous. When we stumble while walking, we usually briefly adjust our clothing, neutralize the shock with a shake of the head, and walk on at a measured pace. The same reaction is appropriate in the case of an acid stumble of the stomach—a couple of mouthfuls of water for adjustment, neutralize the acid if necessary, and then continue walking, perhaps at a less hectic pace.

Vomiting

IF YOU TOOK a hundred people on the verge of vomiting, you would have a very mixed group. Person number 14 is on a rollercoaster, hands high in the air, person 32 is cursing the egg salad she ate, number 77 is holding a pregnancy test in disbelief, and number 100 has just read the words “may cause nausea and vomiting” in the leaflet that came with his new medication.

Vomiting is not a stomach stumble: it happens according to a precise plan. It is a tour de force performance. Millions of tiny receptors test our stomach contents, examine our blood, and process impressions from the brain. Every piece of information is gathered in the huge fibrous network of our nervous system and sent to the brain. The brain evaluates this information. Depending on how many alarm bells are ringing, it makes a decision: to barf or not to barf. The brain transmits its decision to selected muscle groups, and they get down to work.

If you were to X-ray the same hundred people while they were vomiting, the picture would be the same a hundred times over. The brain responds to the alarm, activates the area responsible for vomiting, and switches the body to emergency mode. We turn pale as the blood drains from our cheeks and is sent to the abdomen. Our blood pressure drops and our heart rate falls. Finally, we feel that unmistakable sign: saliva, and lots of it. The mouth begins producing saliva in great quantities as soon as it receives information from the brain about the emergency that’s underway. This saliva is meant to protect our teeth from the corrosive effects of the gastric acid they are about to come into contact with.

To begin with, the stomach and gut move in small, nervous waves—shoving their contents in completely opposite directions as they begin to panic slightly. We cannot feel this to-and-fro as it takes place in the realm of smooth muscle; however, this is about the time that most people realize intuitively that they should seek out a suitable receptacle.

An empty stomach is no defense against vomiting, since the small intestine is just as able to expel its contents. For this to happen, the stomach

opens the gate to allow the contents of the small intestine back in. Every member of the team works together to bring this major project to completion. When the small intestine suddenly sweeps its contents into the stomach, sensitive nerves there are stimulated. These nerves respond by sending signals to the vomit control center in the brain. Now there's no doubt about it: everything is ready for the big heave.

Our lungs take a particularly large breath before our airways are closed. The stomach and the opening to the esophagus suddenly relax and—bam!—the diaphragm and abdominal muscles abruptly press upward, squeezing us like a tube of toothpaste. The entire contents of the stomach are then propelled from the body like a pilot in an ejector seat.

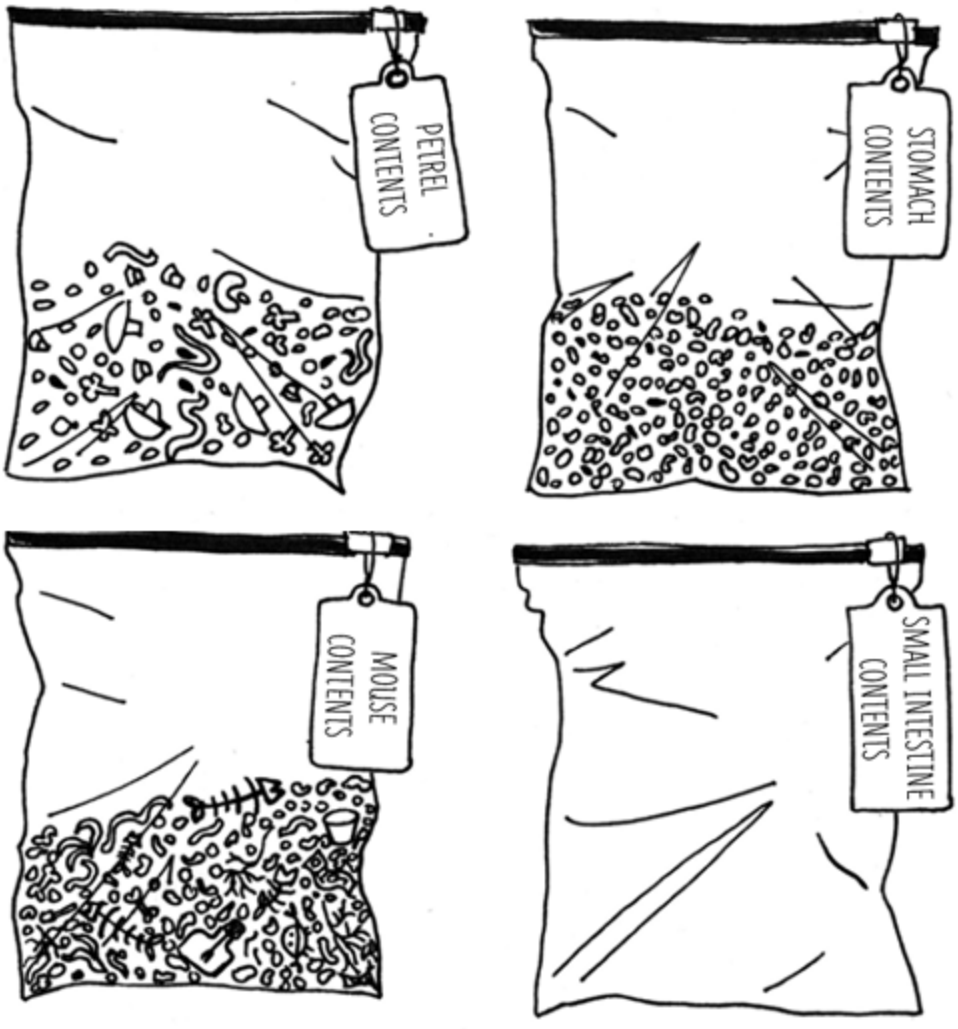
Why We Vomit and What We Can Do to Prevent It

The human animal is especially designed to be able to vomit. Other animals with this ability include apes, dogs, cats, pigs, fish, and birds. Those that are not able to vomit include mice, rats, guinea pigs, rabbits, and horses. Their esophagus is too long and narrow, and they lack the nerves that are so talented at vomiting.

Animals that cannot vomit have to have different eating habits from ours. Rats and mice nibble at their food, biting off tiny pieces to test their suitability. They only continue to eat when they are sure the trial nibble has not done them any harm. If it turns out to be toxic, the most they suffer will be a bout of stomachache. They also learn not to eat it again. Furthermore, rodents are much better than us at breaking down toxins because their liver has more of the necessary enzymes. Horses, however, are not even able to nibble. If something bad ends up in their small intestine, the results can often be life threatening. So, really, we have reason to be proud of our body's abilities whenever we find ourselves crouched over the toilet bowl "throwing our guts up."

The short rests between retches could be utilized for a little reflection. Person number 32's notorious egg salad seems to have held its form surprisingly well when it returns from its short sojourn in the realm of the stomach. A few pieces of egg, the odd pea or piece of pasta are still

recognizable. It might cross 32’s mind that she can’t have chewed it very well. Moments later, another retch produces rather more deconstructed arrangement. Vomit that contains recognizable bits of food is almost certain to have originated from the stomach and not from the small intestine. The smaller the particles, the more bitter the taste, and the more yellow the color, the more likely it is to be a salutation from the small intestine. Clearly identifiable food may not have been chewed properly, but at least it has been ejected from the stomach quickly, before making it as far as the small intestine.



The way we vomit also tells us quite a bit. Sudden vomiting that comes in a violent surge almost without warning is likely to be caused by a gastrointestinal virus. This is due to the fact that the sensors count how

many pathogens they encounter and when they decide the numbers have got out of hand, they slam on the emergency brakes. Below this threshold, the body's immune system could likely have dealt with the situation, but now the job is handed over to the gastrointestinal muscles.

Food poisoning and alcohol poisoning also cause vomiting in surges. However, this time we usually get a fair warning beforehand, in the form of nausea. The feeling of nausea is the body's way of telling us that the food we have eaten is not good for us. Person 32 is likely to be much more wary of that bowl of egg salad on the buffet in future.

Person 14 on the rollercoaster feels just as nauseous as number 32 of egg salad fame. Rollercoaster puking is basically the same as travel sickness. In this case, no toxins are involved, yet sick still ends up on people's shoes, in the glove compartment, or splattered on the back window by the force of momentum. The brain is the bodyguard of the body—guarding it meticulously and cautiously, especially when the body belongs to a small child. Currently, the best explanation of motion sickness is this: when the information sent to the brain from the eyes is at odds with that sent by the ears, the brain cannot understand what is going on and slams on every emergency brake at its disposal.

When a passenger reads a book in a moving car or train, their eyes register "hardly any motion," while the balance sensors in the ears say "lots of motion." It's the same, but opposite, effect as when you watch the trees whizz by when driving through a forest. If you move your head a little as well, it looks as if the trees are rushing by faster than you are actually moving—and that, too, confuses the brain. On an evolutionary scale, our brains are familiar with such mismatches between eyes and balance sensors as signs of poisoning. Anyone who has ever drunk too much or taken drugs will have felt the room spinning, even when they are not moving at all.

Vomiting can also be caused by intense feelings such as emotional strain, stress, or anxiety. Under normal circumstances, we synthesize the stress-response hormone CRF (corticotropin-releasing factor) in the morning, creating a supply to help face the challenges of the day. CRF helps us tap into energy reserves, prevents the immune system from overreacting, and helps our skin tan as a protective response to stress from sunlight. The brain can also inject an extra portion of CRF into the bloodstream if we find ourselves in a particularly upsetting situation.

However, CRF is synthesized not only by brain cells, but also by gastrointestinal cells. Here, too, the signal is—stress and threat! When gastrointestinal cells register large amounts of CRF, irrespective of where they originate (in the brain or in the gut), the information that one of the two is overwhelmed by the outside world is enough for the body to react with diarrhea, nausea, or vomiting.

When the brain is stressed, vomiting expels partly digested food in order to save the energy required to complete the digestive process. The brain can then use that energy to solve the problems at hand. When the gut is stressed, partly digested food is ejected either because it is toxic or because the gut is currently not in a position to digest it properly. In both cases, it can make good sense to press the eject button. There is simply no time for gentle, comfortable digestion. When people throw up from nerves, it is simply their digestive tract trying to do its best to help.

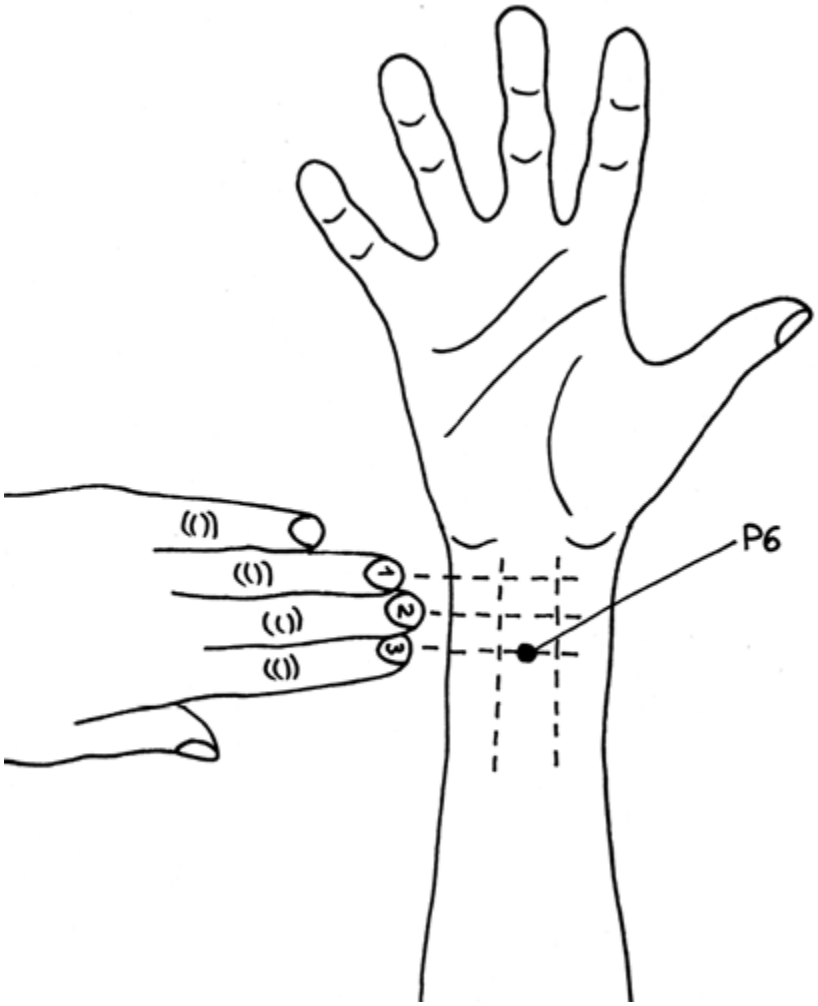
Incidentally, petrels use vomiting as a defense strategy. Vomiting is a sign from the plucky little birds to steer well clear of their nests. Researchers use that to their advantage. They approach a petrel's nest holding out a barf bag, and the seabird pukes right into it. Back at the lab, they can test the petrel vomit for anything from the presence of heavy metals to the variety of fish it contains. This gives them a measure of how healthy the environment is.

THE FOLLOWING INCLUDES some simple strategies for reducing unnecessary attacks of vomiting.

1. For travel sickness, keep your eyes fixed on the horizon far ahead. This helps the eyes and balance sensors coordinate their information better.
2. Listen to music on headphones, lie on your side, or try relaxation techniques—some people find this helpful. One possible explanation for this is that all these activities are generally calming. The more secure we feel, the less we en-courage the brain's state of alarm.
3. There are now quite a few studies proving that ginger has a beneficial effect. Substances contained in root ginger block the vomit center of the brain and the feeling of nausea along with it. Many ginger candies, however, contain only ginger flavoring, so make sure anything you take contains the genuine stuff.
4. Drugs you can buy from the pharmacy to prevent vomiting work in various ways. They can block the receptors in the vomit center (the same

effect as ginger), numb the nerves of the stomach and gut, or suppress certain alarm signals. The drugs in the last group are almost identical to drugs used to treat allergies. Both suppress the alarm-signal transmitter histamine. However, the drugs used to prevent vomiting have a much stronger effect on the brain. Modern allergy drugs have been developed and improved to such a degree that they barely dock in the brain at all. This interaction with the brain is what makes the suppression of histamines cause drowsiness.

5. P6! This is an acupuncture point that is now recognized by Western medicine as effective against nausea and vomiting. Its benefits have been proven in more than forty studies, including placebo-controlled trials. Doctors do not know how or why P6 works. The point is located two to three finger-breadths below the wrist, right between the two prominent tendons of the lower arm. If you don’t happen to have an acupuncture needle handy, you can try gently stroking the skin at that point until symptoms improve. This technique has not been proven in scientific studies, but it may be worth trying a little self-experimentation. In traditional Chinese medicine, stimulating this point is believed to activate the energy pathway, or meridian, running up the arm and through the heart, which relaxes the diaphragm and then runs on through the stomach and into the pelvis.



NOT EVERY STRATEGY will work for all causes of nausea. Remedies like ginger, pharmacy-bought medicines, or P6 can help, but for vomiting caused by emotional factors, the best thing is often to build a safe nest for your own inner petrel. Relaxation techniques or hypnotherapy (from a reputable practitioner!) can help train the nerves to be more thick-skinned. The more often and the longer you practice, the better you will get. Silly stress at the office or exam-related anxiety become less threatening when we refuse to let these stressors affect us so personally.

Vomiting is never a punishment from the stomach! Rather, it is a sign that our brain and our gut are willing to sacrifice themselves to the ultimate extreme for us. They protect us from unseen toxins in our food, are overcareful when faced with travel-related eye–ear hallucinations, and save

energy to deal with imminent problems. Nausea is meant to give us an orientation for the future, letting us know what is good for us and what is bad.

If you are unsure about the cause of your nausea, it is a good idea to simply trust your gut feeling. The same principle applies when you have eaten something bad but don't feel the need to vomit. You should not force the situation with a finger down your throat, by drinking salt water, or by having your stomach pumped. Taking acidic or foaming chemicals can cause more problems than it solves. Foam can easily migrate from the stomach to the lungs, and acidic drugs may simply burn the esophagus for a second time. For these reasons, induced vomiting is no longer a technique normally recommended for use in modern emergency medicine.

True nausea is a program that has evolved over many millennia—it has the ability to wrest the reins of control from our conscious mind. The conscious mind often reacts to this drastic takeover with shock and indignation. It was blithely planning to order another round of tequila shots—and now this? But, since it is often the conscious mind that got the body into this vomitous situation in the first place, it eventually has to back down. If vomiting is caused by an unnecessary, overcautious reaction, the conscience mind can always return to the negotiating table and play its anti-vomiting aces.

Constipation

CONSTIPATION IS LIKE . You wait for something that just won't . And, still you have to use a lot of force. Sometimes, in return for all that effort, you get no more than • • •. Or it works, but not very

often.

Between 10 and 20 percent of people in the United States are constipated. If you want to join this club, you must fulfil at least one of the following conditions: bowel movement less than three times a week; particularly hard stool a quarter of the time, often in pellet form (• • •), which is difficult or impossible to pass without help (medication or tricks); no satisfying feeling of emptiness on leaving the toilet.

Constipation results from a disconnect between the nerves and the muscles of the gut when they are no longer working toward quite the same goal. In most cases, digestion and transportation of food through the system are still working at normal speed. It is not until the very end of the large intestine that disagreement arises as to whether the contents need to be expelled right away or not.

The best parameter for assessing constipation is not *how often* you need to go to the toilet, but *how difficult* it is. Time spent sitting on the toilet is supposed to be a time of splendid isolation and relaxation, but for those whose experience is not so laid back, it can be a troubling time. There are various levels of constipation. Temporary constipation can be due to traveling, illness, or periods of stress. More obstinate constipation can indicate more long-term problems.

Almost half of us have experienced constipation when traveling. Particularly in the first few days of a trip, it is often difficult to go properly. This can be due to a variety of reasons, but in most cases it boils down to the simple fact that the gut is a creature of habit. The nerves of the gut remember what kind of food we prefer and at what time we prefer to eat it. They know how much we move around and how much water we drink.

They know whether it is day or night and what time we usually go to the toilet. If everything goes according to plan, they complete their tasks without complaint and activate our gut muscles to help us digest.

When we travel, we have a lot on our mind. Did we pick up our keys and turn off the iron? We might remember to take a book or some music to keep our brains happy, but there is one thing we always forget—that creature of habit, the gut, is also traveling with us and is suddenly torn from its familiar routine.

We spend the whole day eating prepackaged sandwiches, strange airplane meals, or unfamiliar spices. At the time we would normally be enjoying our lunch break, we're stuck in traffic or waiting at the check-in counter. We drink less than normal, for fear of having to go to the toilet too often, and dehydrate even more during the flight. And, as if that weren't enough, we might also have to face a big fat bout of jetlag.

All this does not go unnoticed by the nerves of the gut. They can get confused and put the brakes on until they receive a signal that everything is normal and they can start work again. Even when the gut has done its work despite the confusion, and signals to us that we should seek out the toilet, we add to its woes by suppressing the urge because it happens not to be a convenient time. Also, if we're honest, travel constipation can often be caused by the "not my toilet" syndrome. Sufferers of this syndrome simply dislike doing their business in unfamiliar toilets. Their biggest challenge is posed by public conveniences. Many people use them only when it's absolutely necessary, construct elaborate seat sculptures out of toilet paper, or crouch what feels like miles away from the toilet bowl. But even all that doesn't help those with a serious case of "not my toilet" syndrome. They simply cannot relax enough to finish the work their creature of habit has begun. When that happens, a holiday or business trip can become a rather unpleasant experience.

THERE ARE A FEW little tricks that can be useful for people with brief or mild instances of constipation. These tricks can lower inhibitions and help get things moving in the bowel department.

1. There is a certain foodstuff we can eat to nudge the gut wall into action: fiber. Dietary fiber is not digested in the small intestine and can knock on the wall of the large intestine in a friendly way to say there is someone

here who wants to be shown the way out. The best results are produced by psyllium seed husks and the rather more pleasant-tasting plum. Both contain not only fiber, but also agents that draw extra fluids into the gut —making the whole business smoother. It can take two to three days before their effect is felt. So, you can start eating them either a day before your trip or on the first day—whatever feels safer. Those with no plum compartment in their suitcase can buy dietary fiber in tablet or powdered form from their pharmacy or drug store. One ounce (30 grams) is an appropriate daily dose of dietary fiber.

There are two kinds of fiber: water-soluble and insoluble. The latter is better at stimulating movement through the digestive system, but it can often cause stomachaches. Water-soluble fiber does not provide quite such a powerful push, but it does make the contents of the gut softer and easier to deal with. Nature's design is rather clever: the skins of many fruits contain large amounts of insoluble fiber, while the flesh of the fruit contains more soluble fiber.

Consuming dietary fiber is little help if you do not also consume sufficient fluids. Without the presence of water, fiber binds together in solid lumps. Water makes them swell up into balls. This gives the bored gut something to do while your brain enjoys the in-flight entertainment.

2. Drinking more fluids can only help those who don't already drink enough. For those who do, drinking even more will not bring about any improvement. But it is a different story if the body gets too little fluid. The gut reacts by extracting more water from the food passing through it. That makes the feces harder. Small children running high temperatures often lose so much body fluid through sweating that their digestive system grinds to a halt. Air travel can cause the body to lose similar quantities of water, even without sweating. The air in the plane is so dry that it extracts fluid from our body without our even noticing. The first sign we have of it is an unusually dry nose. During air travel it is a good idea to try to drink more than normal to keep the water in your body at a normal level.
3. Don't put yourself under pressure. If you need to go to the toilet, just go —especially if you are a creature of habit like your gut and usually go at an appointed time. If you normally go to the toilet in the morning but suppress the urge because you're traveling, it is as if you have broken an

unspoken agreement with your gut. You gut likes to work according to plan. Pushing digested food back into a holding pattern even just a couple of times trains the nerves and muscles to operate in reverse gear. That can make it increasingly difficult to change gears back again. This is compounded by the fact that the longer the feces stay in the gut, the more time the body has to extract fluid from them, making the business ever harder. A couple of days of suppressing the urge can lead to constipation. So, if you still have another week of your camping holiday to go, you'd better get over your fear of the communal toilets before it's too late!

4. Probiotics and prebiotics—living, beneficial bacteria and their favorite food—can breathe new life into a tired gut. It is a good idea to consult your pharmacist about this or turn to the sections on probiotics and prebiotics later in this book.
5. Take more walks? That is not always a successful strategy. A sudden decrease in exercise can cause the gut to slow down, it's true. But for those who already exercise enough, more movement will not help them attain digestive nirvana. Tests have shown that it takes extremely strenuous exercise to achieve a measurable effect on the movement of the gut. So, unless you are planning to engage in some kind of power sport, forcing yourself to take an extra walk will have little effect—on your ability to go to the toilet successfully, at any rate.

THOSE WITH A taste for the unusual might want to try the rocking squat technique. Sitting on the toilet, bend your upper body forward as far as possible toward your thighs, then straighten up to the sitting position again. Repeat this a few times and it should begin to work. No one watches you while you are on the toilet and you have a moment of free time, so what could be a better opportunity for an unusual experiment?

HERE ARE SOME strategies for times when household remedies and rocking on the toilet fail.

In more stubborn cases of constipation, the nerves of the gut are not just confused or sulking, they are in need of a bit more support from their owner. If you have tried all the little tips and still don’t leave the toilet singing a merry tune, it may be time to rummage in another box of tricks. But you should only do this if you already know the reason for your problem. If you don’t know the precise cause of your constipation, you cannot choose the right remedy.

If constipation comes on very suddenly or lasts for an unusually long time, you must consult your doctor. The problems may stem from undiagnosed diabetes or thyroid problems, or you may just be a natural-born slow transporter.

Laxatives

The aim of taking laxatives is easily stated: to produce the perfect little pile. Laxatives can coax even the shyest gut out of its shell. Laxatives come in various types, which work in different ways. For all hopelessly constipated travelers, slow transporters, campsite toilet objectors, or hemorrhoid-hindrance conquerors, here's a look at that box of tricks.

The Perfect Little Pile by Means of Osmosis

... is well formed and not too hard. Osmosis is water's sense of equality. When one region of water contains more salt, sugar, or similar substances than another, the less rich water will flow toward the richer water until both contain the same amount of solute and they can live on in peaceful equilibrium. The same principle helps to revive wilting lettuce—simply soak the sad salad in water and half an hour later your greens will be crispy again. Water flows into the lettuce because its cells contain more salts, sugars, and so on than the pure water in the bowl.

Osmotic laxatives use the same principle of equality. They contain certain salts, sugars, or tiny molecular chains that can travel into the large intestine. Along the way, they gather all the water they can to make the act of going to the toilet as comfortable as possible. But overdoing it with such laxatives causes them to extract too much water. Diarrhea is a sure sign that you have taken too many.

With osmotic laxatives, you can choose whether to take sugars, salts, or short molecular chains to help retain water in the gut. The salts, such as sodium sulfate (also known as Glauber's salt) are rather rough on us. They take effect very suddenly, and if they are taken too often, they disrupt the body's electrolyte balance.

The most widely known laxative sugar is lactulose. It has a useful double effect, both retaining water in the large intestine and feeding the flora of the gut. Those little creatures can help, for example, by producing some substances that act as stool softeners and others that stimulate movement in the gut wall. But this can also cause unpleasant side effects. Overfed or misplaced bacteria can produce gases, causing cramps and flatulence.

Lactulose is formed from the milk sugar, lactose, when milk is heated to high temperatures. Pasteurization involves heating milk briefly, so pasteurized milk contains more lactulose than raw milk. UHT (ultra-high-temperature-processed) milk contains more lactulose than pasteurized milk, and so on. Non-milk laxative sugars are also available, including sorbitol. Sorbitol occurs naturally in some kinds of fruit—plums, pears, and apples, for example. That is one reason for the reputation plums have as a natural laxative and for warnings that too much fresh apple juice can cause diarrhea. Since human beings can barely absorb sorbitol (or lactulose) into their bloodstream, it is often used as a sweetening agent. It then appears on food labels as E420, and this explains why sugar-free cough candies, for example, always include the warning, “Excessive consumption may have a laxative effect.” Some studies have shown that sorbitol has a similar effect to lactulose, but causes fewer side effects overall (no unpleasant wind).

Of all laxatives, the short molecular chains are most easily tolerated by the body. They have the kind of complicated names that molecular chains love—polyethylene glycol, for example, known as PEG for short. They don’t disrupt the body’s electrolyte balance like salts do, and they do not produce wind like sugars do. The length of the chain is often included in the name: PG-3350, for example, is a chain made up of enough atoms to give it the molecular weight 3350. It is much better than PEG-150, because that compound is made of such short chains that they can be inadvertently absorbed by the gut wall. That might not necessarily be dangerous, but it can certainly confuse the nerves of the gut, since polyethylene glycol is definitely not part of our natural diet.

For this reason, short chains like PEG-150 are not contained in laxatives, but they are used in products such as skin cream, where they perform a very similar service—they make the skin more supple. It is unlikely that they are harmful, but the matter is still not finally settled. Laxatives based on PEGs contain only indigestible chains, and for that reason they can be taken over

longer periods without causing problems. The latest studies show there is no risk of addiction or long-term damage. Some studies indicate that these substances can even improve the gut's protective barrier.

Osmotic laxatives work not only by making the feces moister, but also by sheer mass. The more moisture, well-fed gut bacteria, or molecular chains are contained in the gut, the more motivated it will be to move. This is the basic principle of the peristaltic reflex.

The Perfect Little Pile by Means of Slippery Stool

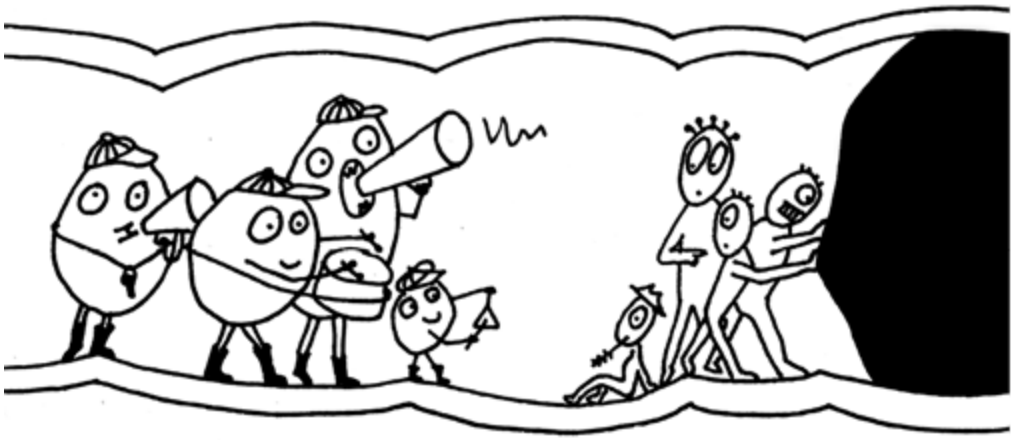
... sounds like a children's party game. Slippery stool—lots of fun but maybe quite messy. But in fact this is the technique known medically as fecal lubrication. Robert Chesebrough, the man who invented Vaseline®, swore by a spoonful of the petroleum jelly every day. Swallowing petroleum jelly probably has the same effect as swallowing other fat-based fecal lubricants—an overdose of indigestible fat coats the goods in transit, making for an easier exit. Chesebrough lived to the ripe old age of ninety-six, which is quite surprising since eating a fat-based lubricant every day will cause the body to lose too many fat-soluble vitamins. They get covered in the fatty lubricant and go the same way as the feces. This can cause vitamin deficiencies that lead to illness, especially if fecal lubricants are taken too often or in excessive amounts. Petroleum jelly is not one of the official fecal lubricants (and really shouldn't be eaten), but the time-honored candidates such as liquid paraffin are hardly less suitable for regular use. They can be useful as short-term treatments—for example, in the presence of hemorrhoids or small but painful injuries to the anus. In such cases, it can be good to make the feces softer to avoid pain or further injury during defecation. However, gel-forming fibers available from the pharmacy do just as good a job and are less dangerous and better for the body.

The Perfect Little Pile by Means of Hydragogues

... is achieved by giving the gut a big kick up the butt. These laxatives are ideal for those with very shy, lethargic gut nerves. There are various tests to find out whether that applies to you. One test involves swallowing little medical pellets that doctors then X-ray as they pass through the gut. If, after a certain time, the pellets are still spread throughout the tract, having failed

to gather by the back door as they should, hydragogues are the appropriate treatment.

Hydragogues latch onto a couple of the receptors that the gut waves around inquisitively. They then send signals to the gut to stop extracting fluid from the food passing through and to fetch more water from other parts: muscles—shake a leg! To put it bluntly, cleverly constructed hydragogues simply boss nerve cells and water transporters around. When osmotic laxatives fail to provide enough stimulus or softness, a shy gut needs a few clear commands. If hydragogues are taken before bedtime and left to do their thing overnight, the gut will react the next morning. If time is an issue, the express mail service of a suppository can usually deliver the message within half an hour.



Hydragogues encourage the gut to keep things moving in the right direction.

The commando squad need not rely on chemical weapons—some plants work in much the same way. These include aloevera and senna, for example. But they do have one rather interesting side effect. Anyone who has ever wished to dye the inside of their gut black is welcome to have a go. This discoloration is not dangerous, and it fades with time.

However, some scientists have reported effects of an excess of hydragogues or aloe vera that would be rather less fun—if they turn out really to be caused by those substances—as they include damage to the nerves. The reason is that nerves that are bossed around too much eventually become overwrought. When that happens, they withdraw into

themselves, like snails when you tap their feelers. For this reason, patients with longterm problems should not take hydragogues more than every two or three days.

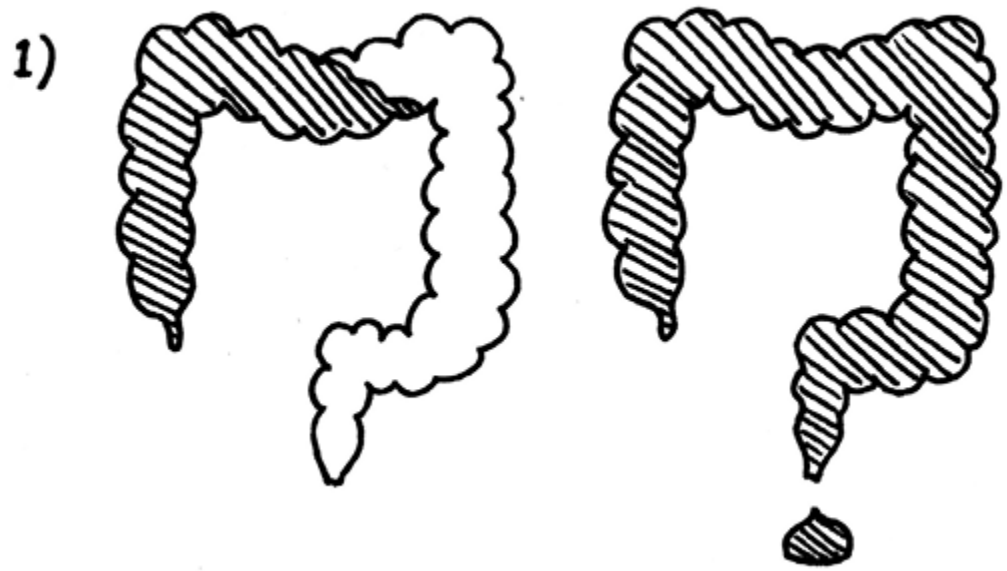
The Perfect Little Pile by Means of Prokinetics

. . . is the very latest thing—for two reasons. These drugs can only support the gut in doing what it naturally does anyway, and they cannot issue any unwanted orders. They work along the same lines as a loudspeaker. The exciting thing for many scientists is that they can help in an extremely targeted way. Some prokinetic agents affect only one single receptor, while others are not absorbed into the bloodstream at all. However, scientists are still researching the way many of these substances work, and new ones are just now appearing on the market. So, anyone who does not absolutely need to try something new should stay on the safe side and rely on better-tested drugs for now.

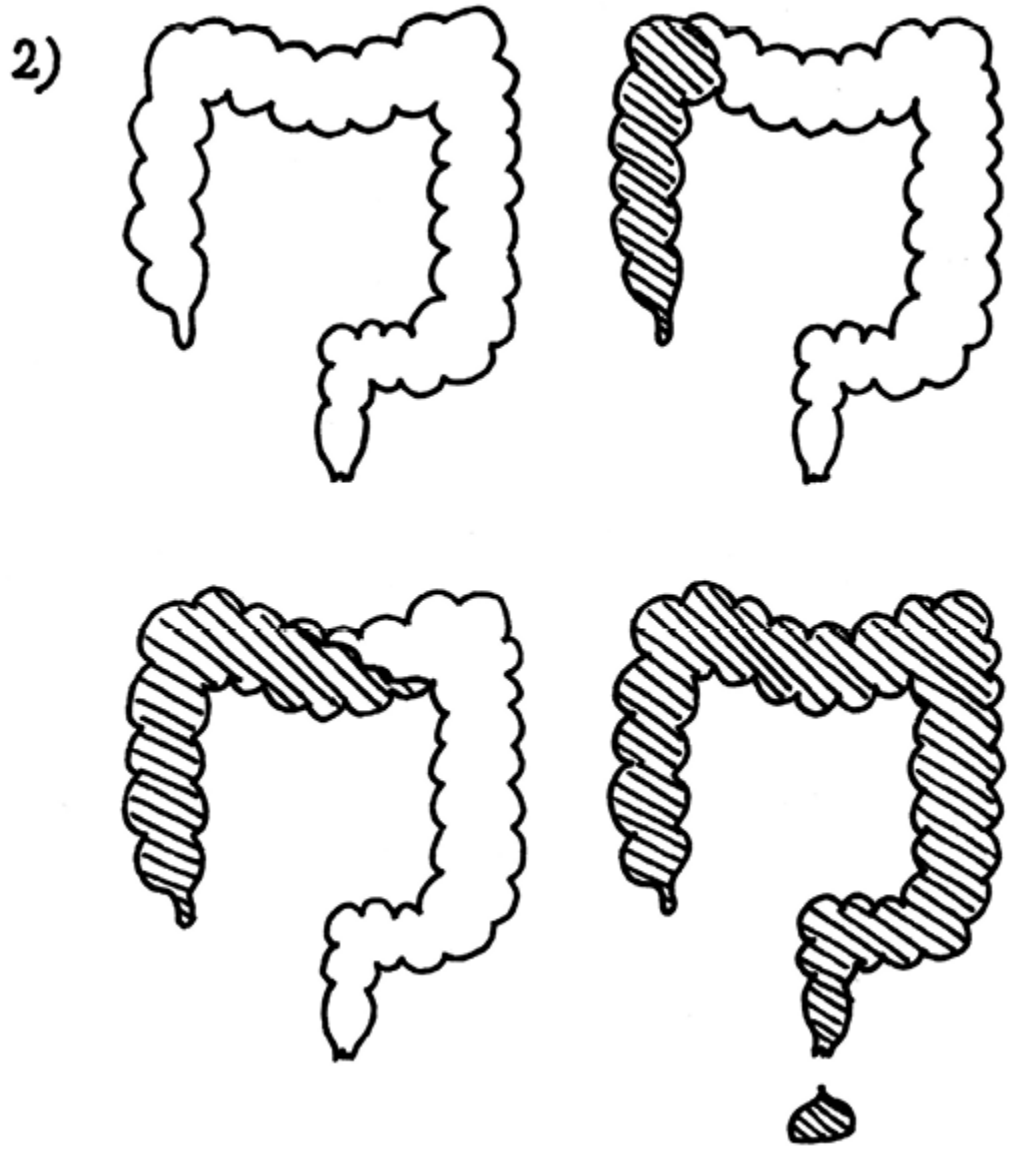
The Three-Day Rule

Many doctors prescribe laxatives without explaining the threeday rule, although it is easy to remember and is a useful aid. The large intestine has three sections: the ascending, transverse, and descending colon. When we go to the toilet, we usually empty the last section. By the next day, it has filled up again and the game starts all over again. Taking a strong laxative may cause the entire large intestine—all three sections—to be emptied. It can then easily take three days before the large intestine is full again.

Those unfamiliar with the three-day rule will likely start to get nervous during that time. Still no bowel movement? And before they know it, they've taken the next laxative tablet or powder. This is a vicious and unnecessary circle. After taking a laxative, the gut deserves a couple of days' respite. Monitoring for normal bowel movements should begin on the third day. Slow transporters may need to give a helping hand to their gut after two days.



1. Normal situation: one-third of the large intestine is emptied and it is full again by the next day.



2. After taking a laxative: the entire large intestine is emptied and it may take three days to fill up again.

The Brain and the Gut

THIS IS A sea squirt.

It may be enlightening to learn the sea squirt's view on the necessity of having a brain. The sea squirt, like humans, is a member of the chordate phylum. It has a bit of a brain and a kind of spinal cord. The brain blithely sends messages to the rest of the body via the spinal cord and receives interesting information in return. In humans, for example, it might receive an image of a traffic sign from the eyes; a sea squirt's eyes might tell it when a fish swims by. A human's brain might receive information from the sensors in the skin about whether it's cold outside; a sea squirt's skin sensors can tell its brain about the temperature of the water deeper in the

sea. A human might get information about whether certain foods are good to eat... and so might a sea squirt.

Equipped with all this information, a young sea squirt navigates the great oceans until it finds a rock that is secure, located in water that is just the right temperature, and surrounded by food. Having found a home, the sea squirt settles down. Sea squirts are sessile animals: once they take up residence, they never move again, no matter what happens. The first thing a sea squirt does after setting up home is to eat its own brain. And why not? It's possible to live and be a sea squirt without one.

Daniel Wolpert is not only an engineer and medical doctor who has won many academic honors, he is also a scientist who believes the sea squirt's attitude to having a brain is very significant. His theory is that the only reason for having a brain is to enable movement. On first hearing, that might sound like an annoyingly mundane statement. But perhaps we just consider the wrong things mundane.

Movement is the most extraordinary thing ever developed by living creatures. There is no other reason for having muscles, no other reason for having nerves in those muscles, and probably no other reason for having a brain. Everything that has ever been done in the history of humankind was only possible because we are able to move. Movement is not just walking or throwing a ball. It is also pulling faces, uttering words, and putting plans into action. Our brain coordinates its senses and creates experience in order to produce movement: movement of the mouth or the hands, movement over many miles or over just a few inches. Sometimes, we can also influence the world around us by suppressing movement. But if you're a tree and can't choose whether you move or not, you don't need a brain.

The common or garden sea squirt no longer needs a brain after it has settled in one place. Its time of movement is over, and so its brain is surplus to requirements. Thinking without moving is less useful than having a mouth opening to eat plankton with. The latter influences the balance of nature at least a tiny bit.

We humans are very proud of our particularly complex brains. Thinking about constitutional law, philosophy, physics, or religion is an impressive feat and can prompt extremely sophisticated movements. It is awe-inspiring that our brains are capable of all this. But at some point, that awe wears off, and we hold our brains responsible for everything we experience in life—

we think up experiences of well-being, happiness, or satisfaction inside our own heads. When we are insecure, anxious, or depressed, we worry that the computer in our heads might be broken. Philosophizing and physics research are matters of the mind and always will be—but there is more to our self than that.

And it is from the gut that we learn this lesson—the organ that is responsible for little brown heaps and unbidden sounds and smells of all sorts. This is the organ that is currently forcing researchers to rethink. Scientists are cautiously beginning to question the view that the brain is the sole and absolute ruler over the body. The gut not only possesses an unimaginable number of nerves, those nerves are also unimaginably different from those of the rest of the body. The gut commands an entire fleet of signaling substances, nerve-insulation materials, and ways of connecting. There is only one other organ in the body that can compete with the gut for diversity—the brain. The gut's network of nerves is called the "gut brain" because it is just as large and chemically complex as the gray matter in our heads. Were the gut solely responsible for transporting food and producing the occasional burp, such a sophisticated nervous system would be an odd waste of energy. Nobody would create such a neural network just to enable us to break wind. There must be more to it than that.

We humans have known since time immemorial something that science is only now discovering: our gut feeling is responsible in no small measure for how we feel. We are "scared shitless" or we can be "shitting ourselves" with fear. If we don't manage to complete a job, we can't get our "ass in gear." We "swallow" our disappointment and need time to "digest" a defeat. A nasty comment leaves a "bad taste in our mouth." When we fall in love, we get "butterflies in our stomach." Our self is created in our head and our gut—no longer just in language, but increasingly also in the lab.

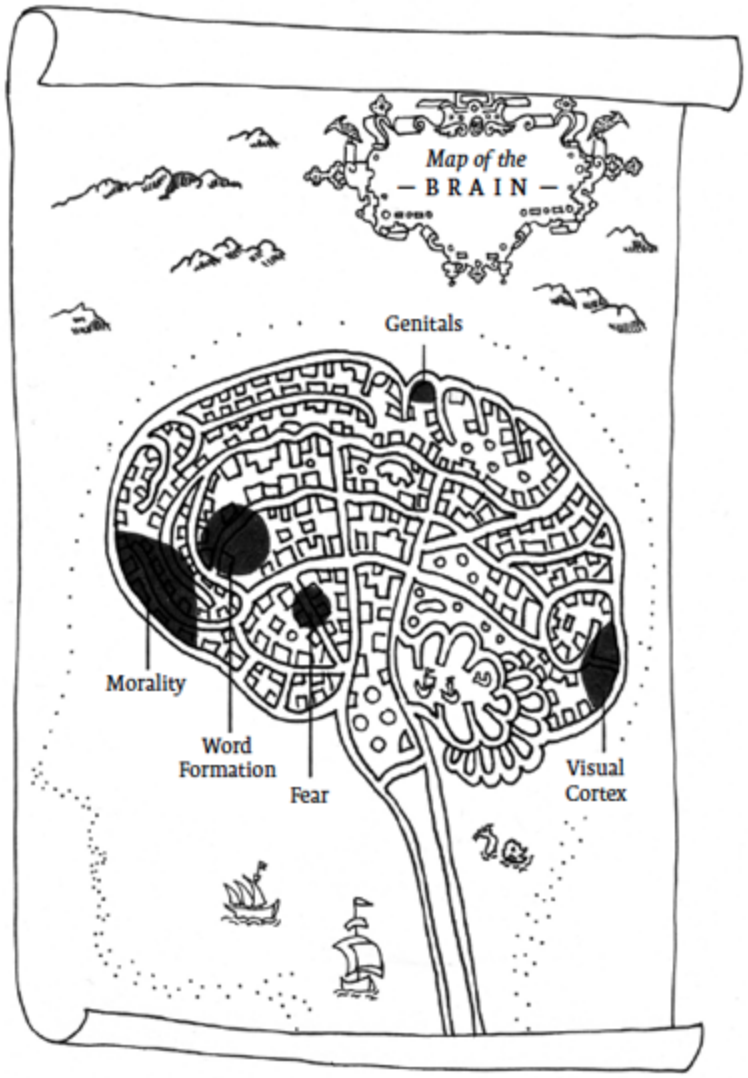
How the Gut Influences the Brain

When scientists study feelings, they start out by looking for something to measure. They draw up scales for suicidal tendencies, test hormone levels to measure love, or set up trials for tablets to treat anxiety. To outsiders, this

often appears less than romantic. In Frankfurt, there was even a study that involved scanning the brains of volunteers while a research assistant tickled their genitals with a toothbrush. Such experiments tell scientists which areas of the brain receive signals from which parts of the body. This helps them draw a map of the brain.

So they now know, for example, that signals from the genitals are sent to the upper central part of the brain, just below the crown. Fear is found in the middle of the brain—right between the ears, so to speak. Word formation is located just above the temple. Morality is located behind the forehead, and so on. In order to improve our understanding of the relationship between the gut and the brain, we must trace their communication pathways. How do signals get from belly to brain, and what effect do they have when they get there?

Signals from the gut can reach different parts of the brain, but they can't reach everywhere. For example, they never end up in the visual cortex at the back of the brain. If they did, we would see visual effects or images of what is going on in our gut. Regions they can end up in, however, include the insula, the limbic system, the prefrontal cortex, the amygdala, the hippocampus, and the anterior cingulate cortex. Any neuroscientists reading this will be up in arms when I roughly define the responsibilities of these brain regions as, respectively, self-awareness, emotion, morality, fear, memory, and motivation. This does not mean that our guts control our moral thinking, but it allows for the possibility that the gut might have a certain influence on it. Scientists need to conduct more laboratory experiments to look more closely at that possibility.



Areas of the brain activated by vision, fear, word formation, moral thought, and genital stimulation.

The forced swimming test, carried out on mice, is one of the most revealing experiments performed in the name of research into motivation and depression. A mouse is placed in a small container of water that is too deep for it to reach the bottom with its feet, forcing it to swim around trying in vain to get to dry land. The question is, how long will it keep swimming in pursuit of its aim? This boils down to one of the basic questions of our existence: how intensely are we prepared to strive for something that we believe exists? That might be something concrete, like dry land beneath our feet or high school graduation. Or it might be something abstract, like satisfaction or happiness.

Mice with depressive tendencies do not swim for long. They simply freeze, apathetically awaiting their fate. It seems inhibitory signals are transmitted more efficiently in their brains than motivational or driving impulses. Such mice also show a stronger reaction to stress. New antidepressants can normally be tested on these mice. If they swim for longer after receiving the medication, it is an indication that the substance under scrutiny might be effective.

Researchers in the team, led by the Irish scientist John Cryan, took this one step further. They fed half their mice with *Lactobacillus rhamnosus* (JB-1), a strain of bacteria known to be good for the gut. Back in 2011, the idea of altering the behavior of mice by changing the contents of their gut was very new. And, indeed, the mice with the enhanced gut flora not only kept swimming for longer and with more motivation, but their blood was also found to contain fewer stress hormones. Furthermore, these mice performed better in memory and learning tests than their unenhanced peers. When scientists severed their vagus nerve, however, no difference was recorded between the two groups of mice.

The vagus nerve is the fastest and most important route from the gut to the brain. It runs through the diaphragm, between the lungs and the heart, up along the esophagus, through the neck to the brain. Experiments on humans have shown that people can be made to feel comfortable or anxious by stimulating their vagus nerve at different frequencies. In 2010, the European Union approved a medical treatment that uses stimulation of the vagus nerve to help patients suffering from depressive disorders. So, this nerve works something like a telephone connection to the switchboard at a company’s headquarters, transferring messages from staff out in the field.

The brain needs this information to form a picture of how the body is doing. This is because the brain is more heavily insulated and protected than any other organ in the body. It nestles in a bony skull, surrounded by a thick membrane, and every drop of blood is filtered before it is allowed to flow through the regions of the brain. The gut, by contrast, is right in the thick of it. It knows all the molecules in the last meal we ate, inquisitively intercepts hormones as they swim around in the blood, inquires of immune cells what kind of day they’re having, and listens attentively to the hum of the bacteria in the gut. It is able to tell the brain things about us it would never otherwise have had an inkling of.

The gut has not only a remarkable system of nerves to gather all this information, but also a huge surface area. That makes it the body's largest sensory organ. Eyes, ears, nose, or the skin pale by comparison. The information they gather is received by the conscious mind and used to formulate a response to our environment. They can be seen as life's parking sensors. The gut, by contrast, is a huge matrix, sensing our inner life and working on the subconscious mind.

Cooperation between the gut and the brain begins very early in life. Together, they are responsible for a large proportion of our emotional world when we are babies. We love the pleasant feeling of a full stomach, get terribly upset when we are hungry, or grizzle and moan with wind. Familiar people feed, change, and burp us. It's palpably clear that our infant self consists of the gut and the brain. As we get older, we increasingly experience the world through our senses. We no longer scream blue murder when we don't like the food at a restaurant. But the connection between gut and brain does not disappear overnight, it simply becomes more refined. A gut that does not feel good might now subtly affect our mood, and a healthy, well-nourished gut can discreetly improve our sense of well-being.

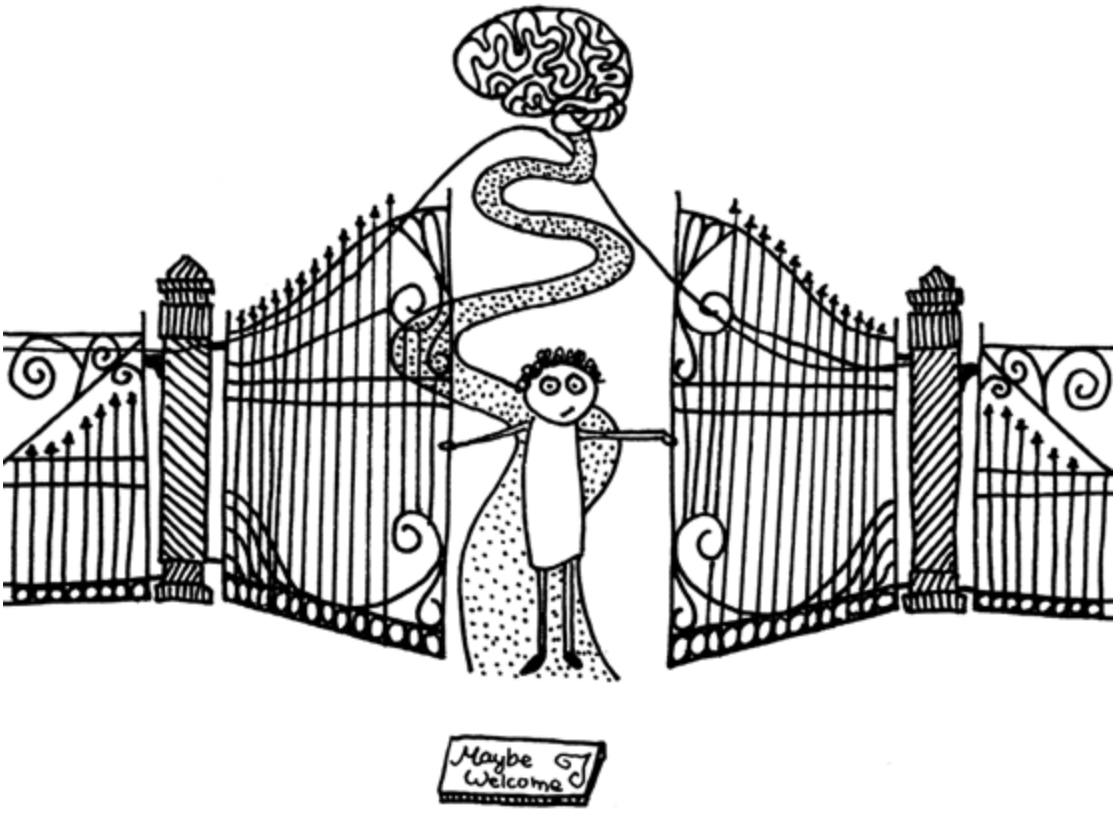
The first study of the effect of intestinal care on healthy human brains was published in 2013—two years after the study on mice. The researchers assumed there would be no visible effect in humans. The results they came up with were surprising not only for them, but for the entire research community. After four weeks of taking a cocktail of certain bacteria, some of the areas of the subjects' brains were unmistakably altered, especially the areas responsible for processing emotions and pain.

Of Irritated Bowels, Stress, and Depression

Not every unchewed pea can intervene in the brain's activity. A healthy gut does not transmit minor, unimportant digestive signals to the brain via the vagus nerve. Rather, it processes them with its own brain—that's why it has one, after all. If it thinks something is important, however, it may consider calling in the brain.

By the same token, the brain does not transfer every piece of information to the conscious mind. If the vagus nerve wants to deliver information to the extremely important locations in the brain, it must get them past the doorman, so to speak. The brain's bouncer is the thalamus. When our eyes report to the thalamus for the twentieth time that the same curtains are still hanging at the living-room window, it refuses entry to that information—it is not important for the conscious mind. A report of *new* living-room curtains is something it would let in, for example. That is not true of everybody's thalamus, but most people's.

An unchewed pea will not make it across the threshold from the gut to the brain. The story is different for other stimuli, however. For example, a report of an unusually large intake of alcohol will make it from the belly to the head, where it informs the vomit control center; information about trapped gas will reach the pain center; and the presence of pathogenic substances will be reported to the officer in charge of nausea. These stimuli make it through because the gut's threshold and the brain's doorman consider them important. But it is not only bad news that makes it across the border. Some signals can cause us to fall asleep on the couch, contented and full after a big Christmas dinner. We are conscious that some of these signals originate from the belly; others are processed in the subconscious areas of the brain and so cannot be located so clearly.



When a gut is irritated, its connection to the brain can make life extremely unpleasant. This shows up on brain scans. In one experiment, the activity in the brains of volunteers was imaged while a small balloon was inflated inside their intestine. Healthy subjects showed normal brain activity with no notable emotional components. When patients with irritable bowels were subjected to the same procedure, however, there were clear indications of activity in the emotional center of the brain normally associated with unpleasant feelings. So the stimulus was able to cross both barriers in those subjects. The patients felt uneasy, although they had not endured anything untoward.

Irritable bowel syndrome is often characterized by an unpleasant bloated feeling or gurgling in the abdomen, and a susceptibility to diarrhea or constipation. Sufferers also have an above-average incidence of anxiety or depressive disorders. Experiments like the one with the balloon show that feeling unwell and negative emotions can arise via the gut–brain axis when the gut's threshold is lowered or when the brain insists on having information it would not normally receive.

Such a state of affairs may be caused by tiny but persistent (so-called micro-) inflammations, bad gut flora, or undetected food intolerances. Despite the wealth of recent research, some doctors still dismiss patients with irritable bowel syndrome as hypochondriacs or malingerers because their tests show no visible damage to the gut.

Other diseases affecting the bowel are different. During an acute phase of their condition, patients with a chronic inflammatory bowel disease like Crohn's disease or ulcerative colitis may have real sores in their bowel wall. With these conditions the trouble is not that even tiny stimuli are transferred from the gut to the brain—their threshold is still high enough to prevent that. The problems are caused by the diseased mucus membrane of the gut. Like patients with irritable bowel syndrome, sufferers of these conditions also show increased rates of depression and anxiety.

There are currently very few—but very good—research teams studying how to make the threshold between the gut and the brain less porous. This is important not only for patients with intestinal problems, but for all of us. Stress is thought to be among the most important stimuli discussed by the brain and the gut. When the brain senses a major problem (such as time pressure or anger), it naturally wants to solve it. To do so, it needs energy, which it borrows mainly from the gut. The gut is informed of the emergency situation via the sympathetic nerve fibers, and is instructed to obey the brain in this exceptional period. It is kind enough to save energy on digestion, producing less mucus and reducing the blood supply.

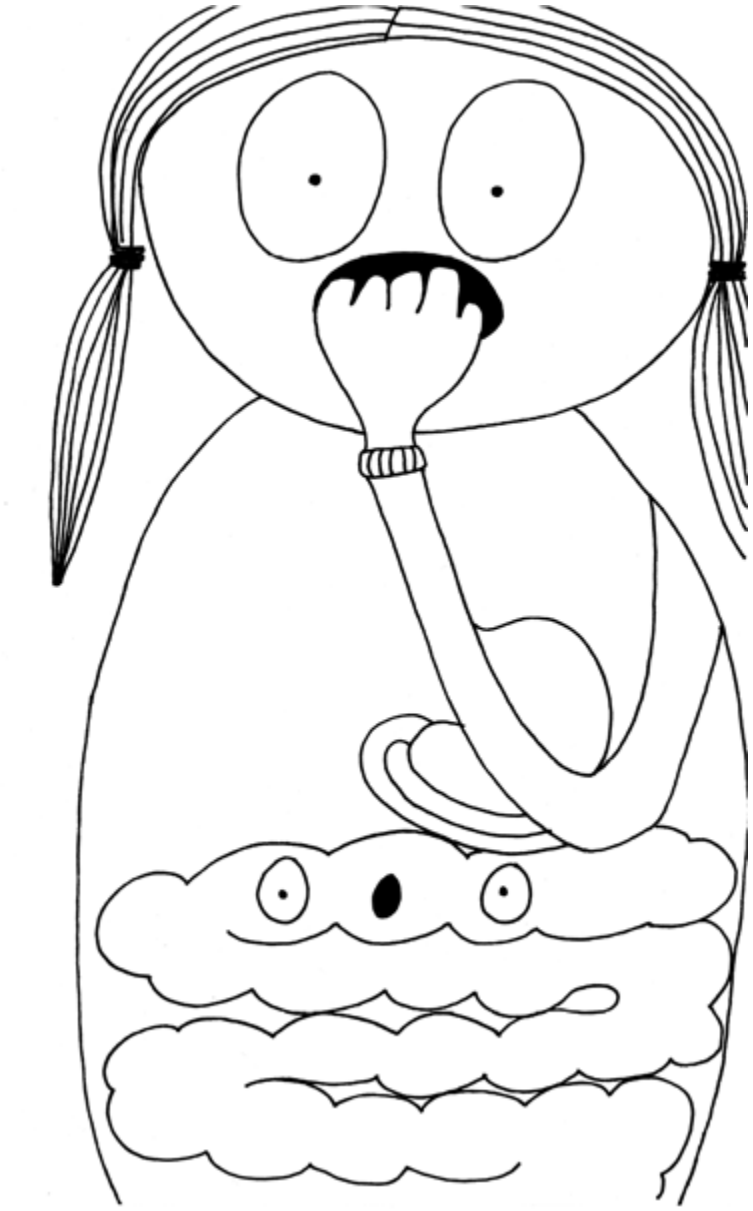
However, this system is not designed for long-term use. If the brain permanently thinks it is in an emergency situation, it begins to take undue advantage of the gut's compliance. When that happens, the gut is forced to send unpleasant signals to the brain to say it is no longer willing to be exploited. This negative stimulus can cause fatigue, loss of appetite, general malaise, or diarrhea. As with emotional vomiting in response to upsetting situations, the gut reacts by ridding itself of food to save energy so it is available to the brain. The difference is that real stress situations can continue for much longer than minor upsets. If the gut has to continue to forego energy in favor of the brain, its health will eventually suffer. A reduced blood supply and a thinner protective layer of mucus weaken the gut walls. The immune cells that dwell in the gut wall begin to secrete large amounts of signal substances, which make the gut brain increasingly

sensitive and lower the first threshold. Periods of stress mean the brain borrows energy, and, as any housekeeper knows, good budgeting is always better than running up too many debts.

One theory proposed by research bacteriologists is that stress is unhygienic. The altered circumstances stress creates in the gut allow different bacteria to survive there than in periods of low stress. We could say stress changes the weather in the gut. Tough guys who have no problem with turbulence will reproduce successfully—and at the end of the day they are not likely to spread good cheer in the gut. If this theory is true, that would make us not just the victims of our own gut bacteria, but also the gardeners of our inner world. It would also mean that our gut is capable of making us feel the negative effects long after the period of stress is over.

Feelings from down below, especially those that leave a nasty aftertaste, will cause the brain to think twice next time about whether it really wants to hold a speech in front of the entire office, or whether we really should eat that super-hot chili. So the process of making decisions based on gut feeling may involve the gut recalling how it felt in similar situations in the past. If positive lessons could also be reinforced in the same manner, then the way to a lover's heart really would be through their stomach—and straight to the gut.

The interesting theory that our gut is not only involved in our feelings and in making "gut decisions" but also may influence our behavior is the subject of various research projects. A team at McMaster University in Canada led by Stephen Collins designed an ingenious experiment using two different strains of mice with very well-researched behavioral characteristics. Members of the strain called BALB/c are more timid and docile than those belonging to the NIH Swiss strain, which exhibit more exploratory behavior and gregariousness. The researchers gave the mice a cocktail of antibiotics that affect only the gut, wiping out their entire gut flora. They then fed the animals with gut bacteria typical of the other strain. Behavior tests showed they had swapped roles—the BALB/c mice became more gregarious and the NIH Swiss mice were more timid. This shows that the gut can influence behavior—at least in mice. The result cannot yet be applied to humans. Scientists know far too little about the various bacteria involved, about the gut brain in general, and about the gut–brain axis.



Until scientists have filled those gaps in their knowledge, we can make use of the facts we already know to improve gut health. It starts with the little things like mealtimes, for example, which should be enjoyed without pressure, at a leisurely pace. The dinner table should be a stress-free zone, with no place for scolding or pronouncements like “You will remain at the table until you’ve finished the food on your plate!” and without constant television channel hopping. This is important for adults, but it is vital for small children, whose gut brain develops in parallel with their head brain. The earlier in life mealtime calm is introduced, the better. Stress of any kind

activates nerves that inhibit the digestive process, which means we not only extract less energy from our food, we also take longer to digest it, putting the gut under unnecessary extra strain.

We can play around with this knowledge and test it experimentally. There are tablets and medicated chewing gum that prevent travel sickness by numbing the nerves of the gut. When the nausea abates, feelings of anxiety often disappear, too. If unaccountable grumpiness or anxiety can originate in the gut (even without nausea), is it possible that these drugs could be used to banish them? By temporarily numbing a troubled gut, so to speak? Alcohol reaches the nerves of the gut before it reaches those in the brain—so how much of the relaxing effect of that "just one glass of wine" in the evening actually comes from a sedated gut brain? What about the array of bacteria in the wide range of yogurt on our supermarket shelves? Is *Lactobacillus reuteri* better for me than *Bifidobacterium animalis*? A team of Chinese researchers managed to show in the laboratory that *Lactobacillus reuteri* is able to inhibit pain sensors in the gut.

Lactobacillus plantarum and *Bifidobacterium infantis* could already be recommended as a pain treatment for patients with irritable bowel syndrome. Many patients with a low pain threshold in the gut currently take substances designed to treat diarrhea, constipation, or cramps. That might help with the symptoms, but it does not address the cause of the problem. If, after eliminating possible food intolerances and restocking the gut flora, there is still no improvement, then we must take the problem by the scruff of its neck—or in this case, by the nerve-cell threshold. So far, very few treatments have been scientifically proven to be effective. One of those is hypnotherapy.

Really good psychotherapy is like physiotherapy for the nerves. It eases tensions and teaches us how to move in a more healthy way—at the neural level. Because the nerves of the brain are more complicated creatures than the muscles of the body, a trainer needs to have more creative exercises up his sleeve. Hypnotherapists often use thought journeys and guided imagery techniques. These aim to reduce the intensity of pain signals and alter the way the brain processes certain stimuli. Just like muscles, certain nerves can become stronger with increased use. The therapy does not involve hypnotism as seen in television shows. That would, in fact, be self-defeating, since this kind of therapy relies on the patient being in control at

all times. Patients must make sure the hypnotherapist they choose is recognized by a reputable institution.

Hypnotherapy has been shown to be effective in treating patients with irritable bowel syndrome, reducing their reliance on medication—in some cases to zero. This is particularly true of children with this condition. For them, hypnotherapy has been shown to produce a 90-percent reduction in pain, compared with a 40-percent reduction produced by drugs. Some clinics offer specific hypnotherapy for abdominal complaints.

Patients with intestinal disease who also suffer from extreme anxiety or depressive disorders are often recommended antidepressants by their doctor. However, they are rarely told why. And there is a simple reason for that: no doctor or scientists knows. It was not until they noticed the mood-enhancing effects of these drugs that scientists began to explore the mechanisms behind this phenomenon. They still have not come up with a clear answer. For decades, it was thought to be due to an enhancing effect of the so-called happiness hormone serotonin. More recently, depression researchers have also begun investigating another possibility—that such drugs may increase the plasticity of the nerves.

Neuroplasticity is the nerves' ability to change. It is nerve plasticity that makes puberty such a confusing time for an adolescent brain—so much is still being molded into shape. The possibilities are endless and nerves are constantly firing off messages in all directions in a pubescent brain. This process is not complete until we reach the age of about twenty-five. After that, nerves react according to well-rehearsed patterns. Patterns that have proved useful in the past are retained; others are rejected as failures. This explains the disappearance not only of the inexplicable fits of laughter and temper tantrums of the teenage years, but also of the posters plastering the bedroom walls. After this age, we find it more difficult to deal with sudden change, but the payback is a more stable, calmer disposition. This can also result in negative thought patterns taking root, such as "I am worthless" or "Everything I do goes wrong." The nervous messages from a worried gut can also become embedded in a person's mind. If it is the case that antidepressants increase neuroplasticity, they may work by loosening up such negative thought patterns. This is most beneficial when accompanied by effective psychotherapy to help patients resist slipping back into old habits.

The side effects of commercially available antidepressants, such as Prozac, also provide us with important clues about the so-called happiness hormone serotonin. A quarter of patients report typical side effects such as nausea, an initial phase of diarrhea, and constipation when the drug is taken over a long period of time. This is explained by the fact that our gut brain possesses the same neural receptors as the brain in our head. So, antidepressants automatically treat both brains. The American researcher Dr. Michael Gershon takes this line of thought one stage further. He is interested in the possibility of developing effective antidepressants that only influence the gut and do not have an effect on the brain.

That is not as outlandish as it might first seem. After all, 95 percent of the serotonin we produce is manufactured in the cells of our gut, where it has an enormous effect on enabling the nerves to stimulate muscle movement and acts as an important signaling molecule. If its effects on the gut can be changed, the messages sent from there to the brain would also be changed enormously. This would be particularly useful in treating the sudden onset of severe depression in people whose lives are otherwise fine. Perhaps it is their gut that needs a session on the therapist's couch and their head is not to blame at all.

Anyone who suffers from anxiety or depression should remember that an unhappy gut can be the cause of an unhappy mind. Sometimes, the gut has a perfect right to be unhappy—if it is dealing with an undetected food intolerance, for example. We should not always blame depression on the brain or on our life circumstances—there is much more to us than that.

Where the Self Originates

Grumpiness, happiness, insecurity, well-being, and worry do not originate in isolation in the mind. We are human beings, with arms and legs, genitals, a heart, lungs, and a gut. Science's concentration on the brain has long blinded us to the fact that our self is made up of more than just our gray matter. Recent gut research has contributed significantly to a new, cautious questioning of the philosophical proposition "I think, therefore I am."

One of the most fascinating parts of the brain that can receive information from the gut is the insula, or insular cortex. This part of the brain is studied by one of the most brilliant brains working in research today: Bud Craig. With super-human patience, he has spent the last twenty years staining nerve fibers and tracking their paths through the brain. Eventually, he emerged from the lab and gave a one-hour talk revealing his theory that human self-awareness originates in the insular cortex.

The first part of his hypothesis goes like this. The insula receives information about feelings from the entire body. Each piece of information is like a pixel. The insula then organizes these pixels to form an overall image. This image is important because it represents a map of our feelings. So, when we are sitting on a chair, we feel the cheeks of our behind pressed against the seat, and we might also feel cold or hungry, for example. Taken together, this gives the overall picture of a cold, hungry person sitting on a hard chair. We might not find this image particularly great, but it is also not awful—it's just okay.

Hypothesis, part two. Daniel Wolpert tells us the purpose of the brain is to create movement—irrespective of whether you are a sea squirt searching for a comfy rock beneath the sea or a human being striving for the best life possible. The aim of movement is to bring about an effect. The brain can use the insula's map to plan meaningful movement. If I am sitting around feeling cold and hungry, other areas of the brain will be motivated to do something to change my situation. I could start shivering, or I could get up and head for the fridge in search of food. One of the main purposes of movement is to shift us constantly toward a healthy equilibrium—from cold to warm, from sad to happy, or from tired to alert, for example.

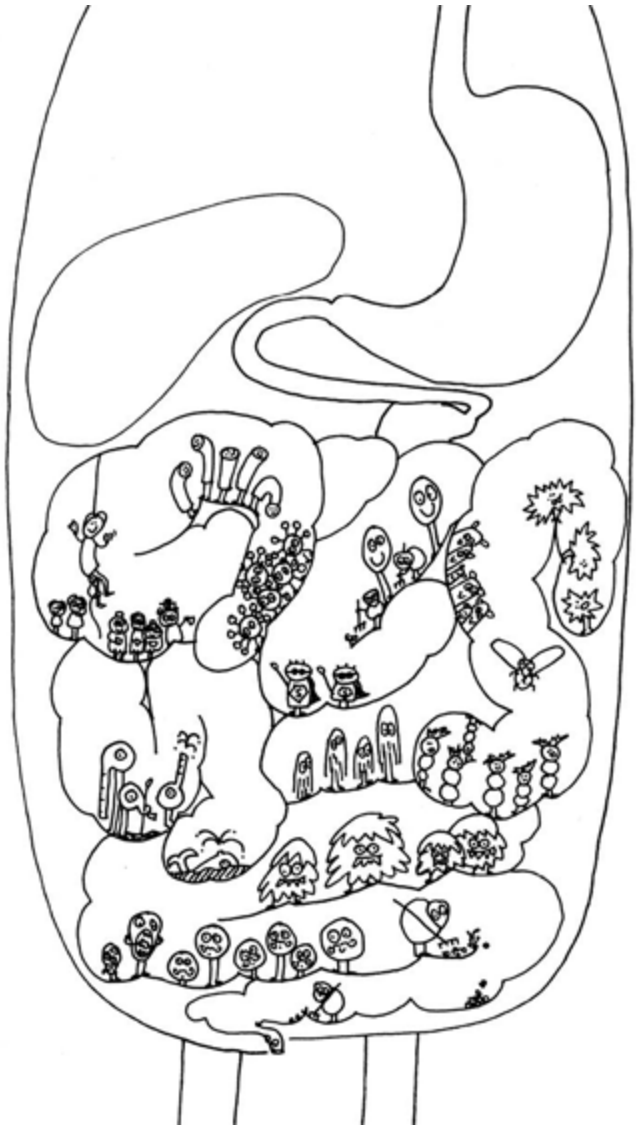
Hypothesis, part three. The brain is an organ of the body. So, if the insula creates an image of the body, that image must also include the on-board computer in our head. It has some interesting areas, such as those responsible for social empathy, morality, and logic. The social areas of the brain might give rise to negative feelings when we argue with our partner; logic regions might induce despair when we try to solve a difficult puzzle. In order for the insula to create a reasonable image of our self, it probably also takes in perceptions of our environment and experiences from the past. So, when we are cold, we don't just feel the low temperature, we are able to contextualize the feeling and think such thoughts as "This is weird. I'm

cold, but I’m in a well-heated room indoors. Maybe I’m coming down with something?” Or alternatively, “Okay, maybe I shouldn’t be parading around naked in the conservatory in winter.” In this way, humans are able to react to the stimulus of feeling cold in a much more complex way than other animals.

The more information we connect, the cleverer the movements we can make. In this respect, there is probably also a hierarchy among our organs. Information that is particularly important for the maintenance of a healthy equilibrium has more sway in the insula. The brain and the gut are well qualified to take a central role—if not *the* central role.

So, the insula creates a picture of our entire feeling body. We can then use our complex brain to embellish this image. Bud Craig believes the picture is refreshed approximately every forty seconds. Through time, those images merge into a kind of movie—the film of the self, of our life.

A great deal of what makes up this movie is certainly contributed by the brain—but not everything. It may be time to expand René Descartes’ proposition: “I feel, then I think, therefore I am.”



(PART THREE)

THE WORLD OF MICROBES

LOOKING DOWN ON Earth from space, it is impossible to make out any human beings. The Earth itself is easily identified—a bright, round spot among the other bright spots in the darkness of space. Closing in a little, it becomes apparent that we humans inhabit all sorts of different places on the planet. Our cities shine at night as patches of light. Some groups are concentrated in big urban centers, others live scattered over wide areas. We inhabit the cool northern climes of Europe and North America, but we also occupy tropical rain-forests and the margins of arid deserts. We are everywhere, even though we are invisible from space.

Looking closer at human beings, it becomes clear that each of us is a world of our own. Our forehead is a breezy meadow, our elbows are arid wastelands, our eyes are salty lakes, and our gut is the most amazing giant forest ever, populated by the weirdest of creatures. Just as we humans occupy the planet, our bodies are occupied by a population that reveals itself only under the microscope—bacteria. Viewed at great magnification, they resemble bright, little spots against a dark background.

For many centuries, humans concerned themselves with the human-sized world. We measured it, examined its flora and fauna, and philosophized about life. We constructed huge machines and flew to the Moon. Explorers keen to discover new continents today must turn to the microscopic world within us. Our gut is perhaps the most fascinating continent of that world. It provides the habitat for more species and families of creatures than any other landscape. Exploration of this region is only now beginning in earnest. A new sense of excitement is brewing among scientists, not unlike that associated with the decoding of the human genome and all the promise that holds for the future. Of course, this excitement about gut research could still fizzle and come to nothing.

Work on an atlas of human bacteria did not begin until 2007. This project involves taking cotton swab samples from all over the bodies of lots and lots of people. Samples are collected from three different areas of their mouths, under their armpits, and on their foreheads. Stool samples are analyzed and genital smears are evaluated. Places once thought to be bacteria-free turn out to be populated after all—the lungs, for example. When it comes to drawing up a bacteria atlas, the gut is the supreme challenge. Of our entire microbiome—that is, all the micro-organisms that

teem on the inside and outside of our bodies—99 percent are found in the gut. Not because there are so few elsewhere, but because there are simply so inconceivably many in the gut.

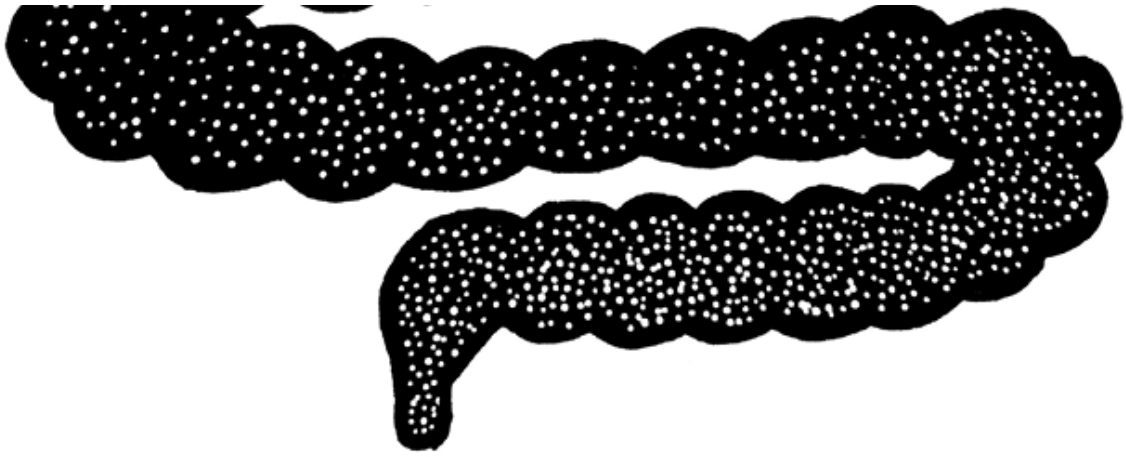
I Am an Ecosystem

WE ARE FAMILIAR with bacteria—those little creatures consisting of a single cell. Some live in boiling hot springs in Iceland, while others luxuriate in the moisture on a dog's wet nose. Some require oxygen to produce energy and "breathe" almost like us and others die when exposed to the fresh air. Those who don't draw their energy from oxygen rely on metal atoms or acids—and that can result in some rather interesting smells. Almost every body smell is, in fact, produced by bacteria. From the pleasant scent of a loved one's skin to the dog-breath of next-door's frisky hound—it is all the product of the microscopic world in us, on us, and around us.

We like to watch athletic surfers as they ride the waves, but we are unaware of the spectacular surfing scenario that takes place in our nasal flora every time we sneeze. We pant and sweat when we exercise, but no one notices how delighted the bacteria who live in our running shoes are over the sudden, summery change in climate. When we take a sneaky bite of cake, we never hear the roar of excited bacteria in our gut, as they gleefully shout, "HERE COMES CA-A-A-KE!" It would take an entire international news agency to report on all the events constantly unfolding in just one person's microbiome. While we lounge about feeling bored, any number of exciting things are happening inside us.

People are slowly beginning to realize that the vast majority of bacteria are harmless, or even helpful. Some facts are now known to science. Our gut's microbiome can weigh up to 4½ pounds (2 kilos) and contains about 100 trillion bacteria. One-thirty-second of an ounce (1 gram) of feces contains more bacteria than there are people on Earth. We also know that this community of microbes cracks open indigestible foodstuffs for us, supplies the gut with energy, manufactures vitamins, breaks down toxins and medications, and trains our immune system. Different bacteria manufacture different substances: acids, gases, fats. You could say bacteria are tiny factories. We know that gut bacteria are responsible for blood groups and that harmful bacteria cause diarrhea.

What we don’t know is what all this means for each individual. We notice pretty quickly when we have ingested diarrhea-causing bacteria. But what do we notice of the work carried out by the many millions, billions, trillions of tiny creatures inside us every day? Does the precise nature of the creatures that colonize us make a difference? Skewed proportions of the different bacteria in our gut have been detected in those suffering from obesity, malnutrition, nervous diseases, depression, and chronic digestive problems. In other words, when something is wrong with our microbiome, something goes wrong with us.



Bacteria population density in the different regions of the gut.

One person might have stronger nerves than another because she has a better stock of vitamin B–producing bacteria. Another person might be able to deal easily with bit of bread mold eaten by mistake. Yet another might have a tendency to gain weight because the “chubby” bacteria in his gut feed him a bit too willingly. Science is just beginning to understand that each of us is an entire ecosystem. Microbiome research is still young, complete with wobbly milk teeth and short pants.

When scientists still knew very little about bacteria, they classified them as plants. This explains terms like gut flora, which is not scientifically accurate, but it is appropriately descriptive. A bit like plants, different bacteria have different characteristics concerning their habitat, nutrition, or level of toxicity. The scientifically correct terms are microbiota (which means “little life”) and microbiome, to refer to our collection of microbes and their genes.

In general, it is accurate to say that the number of bacteria is smaller in the upper sections of the digestive tract, while a very, very large number reside in the lower parts, such as the large intestine and the rectum. Some bacteria prefer the small intestine; others live exclusively in the colon. There are great fans of the appendix, well-behaved homebodies that stick to the mucus membrane, and rather cheekier chaps that nestle up close to the cells of our gut.

It is not always easy to get to know our gut microbes personally. They don’t like to be removed from their own world. When scientists try to grow

them in the lab to observe them, they simply refuse to cooperate. Skin bacteria merrily gobble up the lab food and grow into little microbe mountains—gut bacteria don't. More than half the bacteria that grow in our digestive tract are just too well adapted to living there to be able to survive outside the gut. Our gut is their world. It keeps them warm, moist, protected from oxygen, and supplied with pretasted food.

Only ten years ago, many scientists would probably have maintained that there is a stable stock of gut bacteria that is more or less common to every human being. For example, when they spread feces on a culture medium, they always found *E. coli* bacteria. It was as simple as that. Today, we have machines that can scan tiny amounts of feces molecule by molecule. This reveals the genetic remains of billions of bacteria. We now know that *E. coli* make up less than 1 percent of the population in the gut. Our gastrointestinal tract is home to more than a thousand different species of bacteria—plus minority populations of viruses and yeasts, as well as fungi and various other single-celled organisms.

You might think our immune system would pounce on this multitude of settlers. Defending the body from foreign invasions is high on the immune system's to-do list. Sometimes it even wages war on tiny pollen grains that accidently get sucked into our nostrils. Hay fever sufferers know the signs: a streaming nose and itchy eyes. So, how do the bacteria sidestep the immune system and stage a bacterial Woodstock inside our bodies?

The Immune System and Our Bacteria

WE FACE POTENTIAL death every day. We could get cancer, get eaten away by bacteria, or get infected with a deadly virus. And several times a day, our lives are saved. Strangely mutated cells are destroyed, fungal spores are eliminated, bacteria are peppered with holes, and viruses are sliced in two. This agreeable service is provided by our immune system, with its many little cells. Its workforce includes experts at spotting foreign bodies, contract killers, hatters, and mediators. They all work hand in hand, and together they are a pretty top team.

The vast majority of our immune system (about 80 percent) is located in the gut. And with good reason. This is where the main stage at the bacterial Woodstock is situated, and any immune system worth its salt must be there or be square. The bacteria are confined to a fenced-off area—the mucus membrane of the gut—preventing them from getting too dangerously close to the cells of the gut wall. The immune system can play with the cells without ever posing a danger to the body. This allows our defender cells to get acquainted with many previously unknown species.

If, sometime later and elsewhere in the body, an immune cell encounters a now-familiar bacterium, it can react to it much more quickly. The immune system has to be extremely careful in the gut, suppressing its defensive instincts and allowing the many bacteria there to live in peace. But, at the same time, it must also recognize dangerous elements in the crowd and weed them out. If we decided to say “Hi” to each of our gut bacteria individually, we might just manage it in around 3 million years. Our immune system not only says, “Hi,” it also says, “You’re okay,” or “I’d prefer to see you dead.”

Also, strange as it may sound, the immune system must be able to distinguish between bacterial cells and the body’s own human cells. That is easier said than done. Some bacteria have structures on their surface that bear a close resemblance to those on the surface of our own cells. This is the reason why, for example, scarlet fever should be treated immediately with antibiotics. If it is not treated quickly, the immune system can begin to

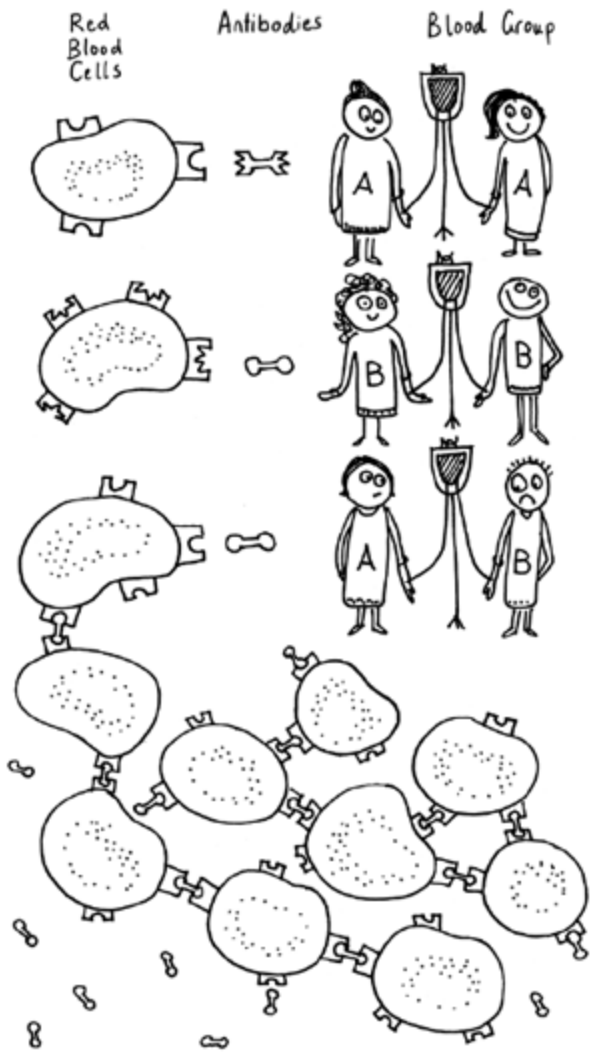
mistake the cells of the joints or other organs for the bacteria that cause scarlet fever and attack them. It might suddenly think our knee is a nasty sore-throat germ hiding out in our leg. It happens rarely—but it does happen.

Scientists have observed a similar effect in patients with juvenile diabetes. Also called diabetes mellitus type 1, this condition results from the autoimmune destruction of the cells that produce insulin. One possible cause is a breakdown of communication with the bacteria of the gut. It may be that they are failing to train the immune system properly or the immune system is somehow getting the message wrong.

The body actually has a very rigorous set of measures designed to guard against such communication breakdowns and cases of mistaken identity. Before an immune cell is allowed to enter the bloodstream, it has to complete the toughest boot camp of any cells. Among other things, it must cover a vast distance while being constantly confronted with various structures of the body. If our little immune cell encounters something it cannot clearly identify as belonging to the body or coming from outside, it stops and prods at it a little. That is a fatal error: this cell will never graduate to the bloodstream.

In this way, immune cells with a tendency to attack the body's own tissue are weeded out before they leave boot camp. In their training center in the gut, they learn to be tolerant of foreign bodies, or rather, they learn to be better prepared for an encounter with them. This system works rather well and usually without untoward incidents.

There is one lesson that is particularly tricky to learn: what to do about foreign bodies that aren't actually bacteria but remind the immune system of them? Red blood cells, for example, have very bacteria-like proteins on their surface. Our immune system would attack our own blood if it had not learned in boot camp that the blood is a no-go area. If our blood cells have the blood-group marker A on their surface, we have no problem receiving transfusions of blood from donors with the same blood group. The reasons for needing a transfusion can be diverse, from a motorbike accident to heavy blood loss during childbirth.



If antibodies match with foreign blood cells, the cells will form clumps. Blood group B has antibodies against blood group A.

However, we cannot receive blood from donors whose blood cells have a different blood-group marker on their surface. It would immediately remind our immune system of bacteria, and since the immune system knows that bacteria have no business being in the bloodstream, it would consider the donated blood cells an enemy and cause the cells to form clumps. If it weren't for this combat readiness—learned through training by our gut bacteria—there would be no blood groups and any donor could give blood to any recipient. For newborn babies, who do not yet have many bacteria in their guts, this is indeed the case. They can theoretically receive

transfusions of blood from any group without any incompatibility effects. (As a precaution, hospitals give babies blood from the mother's blood group, since antibodies from the mother can find their way into the baby's bloodstream.) As soon as babies begin to develop a rudimentary immune system and gut flora, they can only tolerate blood from their own group.

Blood-group development is just one of many immunological phenomena caused by bacteria. There are probably many more waiting to be discovered. Much of what bacteria do tends to be fine tuning. Each kind of bacteria has its own way of affecting the immune system. Some species have been observed to make our immune system more tolerant, for example, by causing more peace-loving, mediatory immune cells to be produced, or by affecting our cells in a similar way to cortisone and other anti-inflammatory drugs. That results in a milder, less belligerent immune system. This is probably a clever move on the part of these tiny creatures, since it increases their chances of being tolerated in the gut.

The fact that the small intestines of young vertebrates (including humans) have been found to contain bacteria that provoke the immune system leaves room for speculation. Could it be the case that these provocateurs help keep the bacteria population in the small intestine down? That would make the small intestine an area of low bacteria tolerance, giving it some peace and quiet for a while. The provocateurs themselves do not hang out in the mucus membrane like good little bacteria, but dock firmly onto the villi of the small intestine. A similar preference is shown by pathogens such as harmful versions of *E. coli.* When they want to colonize the small intestine, but find their favorite places occupied by such provocateurs, they have no choice but to leave.

This effect is known as colonization resistance. The majority of the microbes in our gut protect us simply by occupying spaces that would otherwise be free for harmful bacteria to colonize. Incidentally, the provocateurs of the small intestine belong to that group of characters that refuse to be cultivated outside the gut. How can we be sure that they are not actually harming us? Well, we can't. It is possible that they do harm some people by overstimulating the immune system. Many questions remain to be answered.

Some of those questions might be answered with the help of a group of germ-free mice in a New York laboratory. They are the cleanest creatures in

the world: they come into the world via sterile cesarean births, they live in antiseptic cages, and they eat steam-sterilized food. Disinfected animals like these could never exist in nature. Anyone working with these mice must take the utmost care, since even unfiltered air teems with flying germs. The mice allow researchers to watch what happens to an immune system that has nothing to do. What goes on in a gut with no microbes? How does an untrained immune system react to pathogens? What differences are so obvious they can be seen by the naked eye?

Anyone who has ever had anything to do with such animals will tell you—germ-free mice are weird. They are often hyperactive and exhibit an un-mouse-like lack of caution. They eat more than their germ-colonized peers and take longer to digest their food. They have hugely enlarged appendixes, shriveled digestive tracts with few villi and blood vessels, and a reduced number of immune cells. They are easy prey for even relatively harmless pathogens.

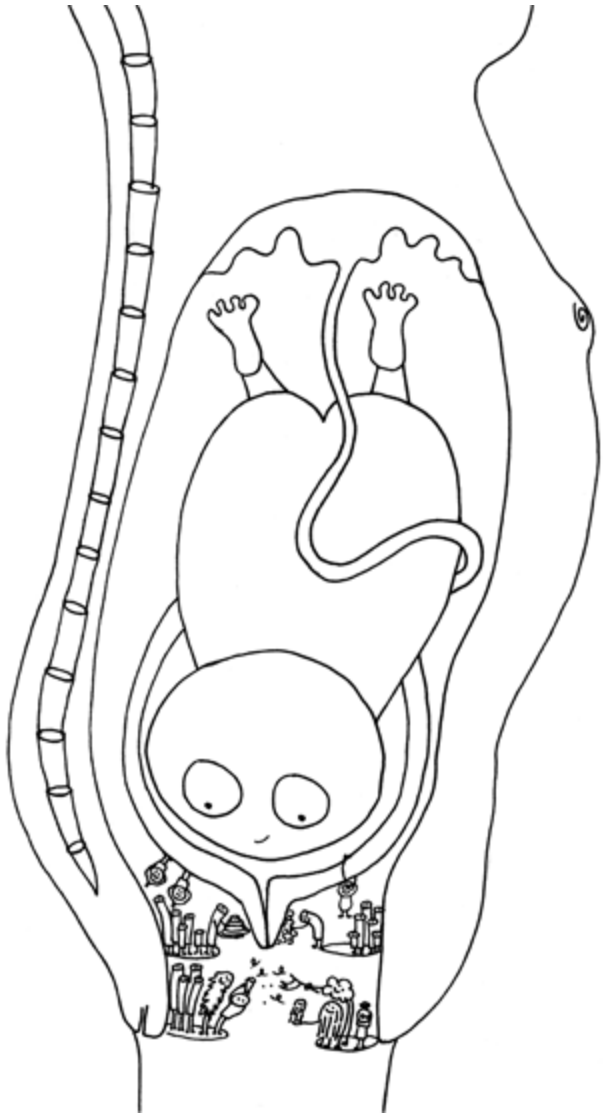
Feeding them with cocktails of bacteria taken from other mice produces astonishing results. If they are given bacteria from mice with type 2 diabetes, they soon begin to develop problems metabolizing sugar. If bacteria from obese humans are fed to germ-free mice, the mice are more likely to gain weight than if they receive bacteria from people in the normal weight range. Scientists can also administer a single species of bacteria to observe its effect on the mice. Some bacteria, acting alone, can reverse the effects of the sterile environment—cranking up the immune system, shrinking the mice's swollen appendixes down to normal size, and normalizing their eating behavior. Other lone bacteria have no effect whatsoever. Yet others take effect only in cooperation with colleagues from other bacteria families.

Studies using these mice have advanced our knowledge quite considerably. We now have good reason to speculate that, just as the macroscopic world we live in influences us, we are also influenced by the microscopic world that lives in us. This is all the more interesting when we realize that each person's inner world is unique to him or her.

The Development of the Gut Flora

AS UNBORN BABIES, we live in an environment that is normally completely germ-free—the womb. For nine months, we have no contact with the outside world except through our mother. Our food is predigested, our oxygen is prebreathed. Our mother's lungs and gut filter everything before it reaches us. We eat and breathe through her blood, which is kept free of germs by her immune system. We are sheathed in an amniotic sac and encased in a muscly uterus that is corked with a thick plug like a big earthenware jug. All this means not a single parasite, virus, bacterium, or fungus—and certainly no other person—can touch us. We are more sterile than an operating table flooded with disinfectant.

This situation is unusual. Never again in our lives will we be so protected and so isolated. If we were designed to remain germ-free once we leave the womb, we would be very different creatures. But that is not the case, so all living things of any size have at least one other living thing that helps them in some way and is allowed to live on or in them in return. This explains why our cells are constructed in such a way that bacteria can easily dock with structures on their surface, and it explains why certain bacteria have coevolved with us over many millennia.



As soon as there is any breach in the protective amniotic sac, colonization begins. While 100 percent of the cells that make us up when we start life are human cells, we are soon colonized by so many microorganisms that only 10 percent of our cells are human, with microbes accounting for the remaining 90 percent. We cannot see this, because our human cells are so much larger than those of our new lodgers. Before we look into our mother’s eyes for the first time, the creatures that live in her body cavities have already looked into ours. The first ones we meet are her protective vaginal flora—an army that defends a very important territory. One way it does this is by producing acids that drive away other bacteria and keep the way cleaner and cleaner the closer they are to the womb.

Unlike the flora in our nostrils, which can be made up of around nine hundred different kinds of bacteria, the criteria for life in the birth canal are much stricter. This sorting process leaves women with a useful coating of bacteria, which wraps itself protectively around the sterile body of the baby as it emerges. About half these bacteria are from one genus: *Lactobacillus.* Their favorite pastime is producing lactic acid. This means the only residents that can set up home in the birth canal are those that pass the acid test.

With a routine birth, all we have to do as babies is decide which way to face as we come out. There are two attractive possibilities: toward the back or toward the front. During birth we are exposed to all sorts of skin contact before we are wrapped up in something soft by another person, who is usually wearing latex gloves.

By now, the founding fathers of our first microbial colonies are already in us and on us. These are mainly our mother's vaginal and gut flora, mixed with a few skin-dwelling germs and possibly a few others from the hospital's repertoire. This is a very good mixture to start with. The acid army protects us from harmful invaders, while other bacteria are already starting to train the immune system, and the first, indigestible components of our mother's milk are broken down for us by helpful microbes.

Some of these bacteria take less than twenty minutes to spawn the next generation. What takes us twenty years or more happens in a fraction of the time—a fraction as tiny as the colonists themselves. While our first gut bacterium watches its great-great-great-great grandchild swim by, we have spent just two hours in the arms of our proud new parents.

Despite this rapid population growth, it will be about three years before the gut flora develops to the right level and then stabilizes. Prior to that, our gut is the scene of dramatic power struggles and great bacterial battles. Some folks who find their way into our mouth spread rapidly throughout the gut, only to disappear again just as quickly. Others will remain with us for the rest of our lives. The composition of our gut colony depends partly on our own actions: we might lick our mother's skin, gnaw on a chair leg, and give the car window or the neighbor's dog the occasional sloppy kiss. Anything that finds its way into our mouth in the process could soon be building its empire in the world of our gut. Whether it will continue to prevail will remain to be seen. And whether its intentions are good or bad

will also remain to be seen. So, we could say we gather our own fate with our mouth. Stool samples can show what comes out the other end. It's a game with many unknowns.

We receive some help creating this collection—mainly from our mother. No matter how many sloppy kisses we give to the car window, if we are allowed to kiss and cuddle with our mother regularly, we will be protected by her microbes. Breast-feeding also promotes particular members of our gut flora—breast-milk-loving *Bifidobacteria*, for example. Colonizing the gut so early, these bacteria are instrumental in the development of later bodily functions, such as those of the immune system or the metabolic system. Children with insufficient *Bifidobacteria* in their gut in their first year have an increased risk of obesity in later life compared with infants with large populations.

There are many, many kinds of bacteria—some beneficial, others less so. Breast-feeding can help shift the balance toward the beneficial and reduce the risk of a later gluten intolerance, for example. A baby's first population of gut bacteria prepares the way for the mature population by removing oxygen and electrons from the intestine. As soon as the environment is free of oxygen, the more typical bacteria of the gut can start to settle there.

Breast milk is so beneficial that a more or less well-nourished mother need not do any more than suckle her baby to ensure it is receiving a healthy diet. When it comes to the nutrients it contains, breast milk provides everything that dietary scientists believe children need in order to thrive—it is the best dietary supplement ever. It contains everything, knows everything, and can do everything necessary for a child's well-being. And, as if that weren't enough, it has the added advantage of passing on a bit of Mom's immune system to her offspring. Breast milk contains antibodies that can protect against any dangerous bacteria a child might make the acquaintance of (by licking the family pet, for example).

Weaning is the first revolution experienced by a baby's gut flora. Suddenly, the entire composition of Junior's food supply is different. Clever old Mother Nature has equipped the typical bacteria that first colonize the infant gut with the genes needed to break down simple carbohydrates such as those in rice. Serve Junior complex, plant-based foods like garden peas, for example, and his baby flora will not be able to deal with them alone. He is now going to need new kinds of digestive bacteria. African children have

bacteria that can manufacture all kinds of tools needed to break down even the most fibrous of plant-based foods. The microbes in the guts of children with a Western diet prefer to avoid such hard work—and they may do so with a clear conscience since their diet consists primarily of puréed baby food and small amounts of meat.

Bacteria do not always manufacture the tools they need—sometimes they also borrow them. In Japan, the gut population has entered into a trade relationship with marine bacteria. They borrowed a gene from their sea-living colleagues that helps break down the kind of seaweed used in Japanese cuisine to make sushi, for example. This shows that the composition of our gut population can depend to a large extent on the tools we need to break down certain foodstuffs.

Useful gut bacteria can be passed on through the generations. Anyone of European heritage who has experienced constipation after a blow-out session at the all-you-can-eat sushi bar will appreciate the advantage of inheriting Japanese seaweed-processing bacteria from someone in the family. However, it is not so easy to infuse yourself or your kids with a few sushi-digesting assistants. Bacteria have to like living in the place where they work.

If we say a microorganism is particularly suited to our gut, we mean it appreciates the architecture of our gut cells, copes well with the climate, and likes the food on the menu. All three of these factors vary from person to person. Our genes help design our bodies, but they are not the chief architects of our microbial home. Identical twins share the same genes, but they do not have the same bacterial mix. They do not even have noticeably more similarities than other pairs of siblings. Our life-style, random acquaintances, illness, or hobbies all influence the shape of the populations inside our body.

On the way to a relatively mature gut flora in our third year, we stick all sorts of stuff into our mouth—some of which will be useful and suited to us. We acquire more and more micro-organisms, building up our population diversity from a couple of hundred species of bacteria to many hundreds of different gut-dwellers. That would be a pretty impressive inventory for any zoo, yet we acquire this variety without even thinking about it.

It is now generally accepted that the first populations to colonize our gut lay the main foundations for the future of our entire body. Studies have

shown the importance of those first few weeks of postnatal bacteria-collecting for the development of the immune system. Just three weeks after birth, the metabolic products of our gut flora can predict increased risks of allergies, asthma, or neurodermatitis in later life. How do we manage to pick up bacteria that are more harmful than beneficial to us so early in life?

More than a third of all children in Western, industrialized countries are brought into the world by means of a convenient cesarean section. No squeezing through a narrow birth canal, no unpleasant side effects like perineal tearing, no delivering the afterbirth—it sounds like a fine thing. The initial contact experienced by children born by cesarean section is mainly with other people's skin. They have to glean bacteria for their gut somehow, since their population will not develop from maternal microbes, like those of children born vaginally. They might end up with bacteria from Nurse Suzy's right thumb, from the florist who sold Daddy that congratulatory bunch of flowers, or from Granddad's dog. Suddenly, factors like the motivation of underpaid hospital cleaners become significant. Did they wipe down the telephones, tables, and bathroom faucets with loving care or a lack of conviction?

Our skin flora is not as strictly controlled as that of the birth canal and is much more exposed to the outside world. Whatever gathers on the skin could soon end up in baby's belly. These uninvited guests may include pathogens or weird types with strange ways of training the young immune system. Children born by cesarean section take months or even longer to develop a normal population of gut bacteria. Three-quarters of newborn babies who pick up typical hospital germs are those born by cesarean section. They also have an increased risk of developing allergies or asthma. One American study showed that administering *Lactobacillus* to those babies can reduce their risk of developing allergies. The same treatment has no effect at all on children born naturally—one could say they were dipped in the probiotic waters of the Styx while they were being born.

By the age of seven, there is barely any discernible difference between the gut flora of children born naturally and those born by cesarean section—the early stages, when the immune and metabolic systems are still impressionable, are long gone. Indeed, cesarean births are not the exclusive cause of less-than-ideal starting populations in the gut. Poor nutrition, unnecessary use of antibiotics, excessive cleanliness, or too much exposure

to bad bacteria can also feature among the causes. In spite of all this, there is no reason for anyone to feel inadequate. We humans are large creatures, and there is no way we can exercise control over every aspect of our microscopic world.

The Adult Gut Population

IN TERMS OF our microbiota, we reach adulthood around the age of three. For a gut, being an adult means knowing how you work and what you like. When that stage has been reached, some gut microbes find themselves on a great expedition with us through our entire lives. We dictate the itinerary—by eating what we eat, reacting to stress, going through puberty, getting ill, and growing old.

Those people who post pictures of their dinner on Facebook, only to be disappointed by the lack of "likes" from friends, are simply trying to appeal to the wrong audience. If there were such a thing as Facebug (Facebook for microbes!), a picture of your dinner would provoke an excited response from millions of users—and shudders of disgust from millions more. The menu changes daily: useful milk digesters contained in a cheese sandwich, armies of *Salmonella* bacteria hiding in a delicious dish of tiramisu. Sometimes we alter our gut flora, and sometimes it alters us. We are our flora's weather and its seasons. Our flora can take care of us, or it can poison us.

We are only now beginning to learn the impact the gut-based bacterial community can have on an adult human. In this respect, scientists know more about bees than about human beings. For bees, having more diverse gut bacteria has been a more successful evolutionary strategy. They were only able to evolve from their carnivorous wasp ancestors because they picked up new kinds of gut microbes that were able to extract energy from plant pollen. That allowed bees to become vegetarians. Beneficial bacteria provide bees with an insurance policy in times of food scarcity: they have no trouble digesting unfamiliar nectar from far-flung fields. More specialized digesters are not so well equipped. Times of crisis highlight the advantage of hosting a good microbial army. Bees with well-equipped gut flora can deal with parasite attacks better than those without. Gut bacteria are an incredibly important factor in this evolutionary survival strategy.

Unfortunately, we cannot simply transfer these results to humans. Humans are not bees; they are vertebrates and they use Facebook. So

researchers have to go back to square one. Scientists investigating our gut bacteria have to learn to understand an almost completely unknown world and its interaction with the world outside. First, they need to know who is living inside our gut.

So let's take a closer look. Who exactly are these characters?

Biologists love to put things in order—from the contents of their own desks to the entire contents of the world. They begin by sorting everything into two large drawers: one for living things and the other for non-living things. They then go on to divide everything in the first drawer into three categories: eukaryotes, Archaea, and bacteria. Representatives of all three groups can be found in the gut. I am not promising too much when I say each of the three groups has its own kind of charm.

Eukaryotes are made up of the largest and most complex cells. They can be multicellular and grow to a pretty impressive size. A whale is a eukaryote. Humans are eukaryotes. Ants are too, incidentally, although they are much smaller than we are. Modern biologists divide eukaryotes into six subgroups: crawly amoeboid microbes, microbes with pseudopodia (foot-like protrusions that aren't real feet), plant-like organisms, single-celled organisms with little mouth-like feeding grooves, algae, and opisthokonts.

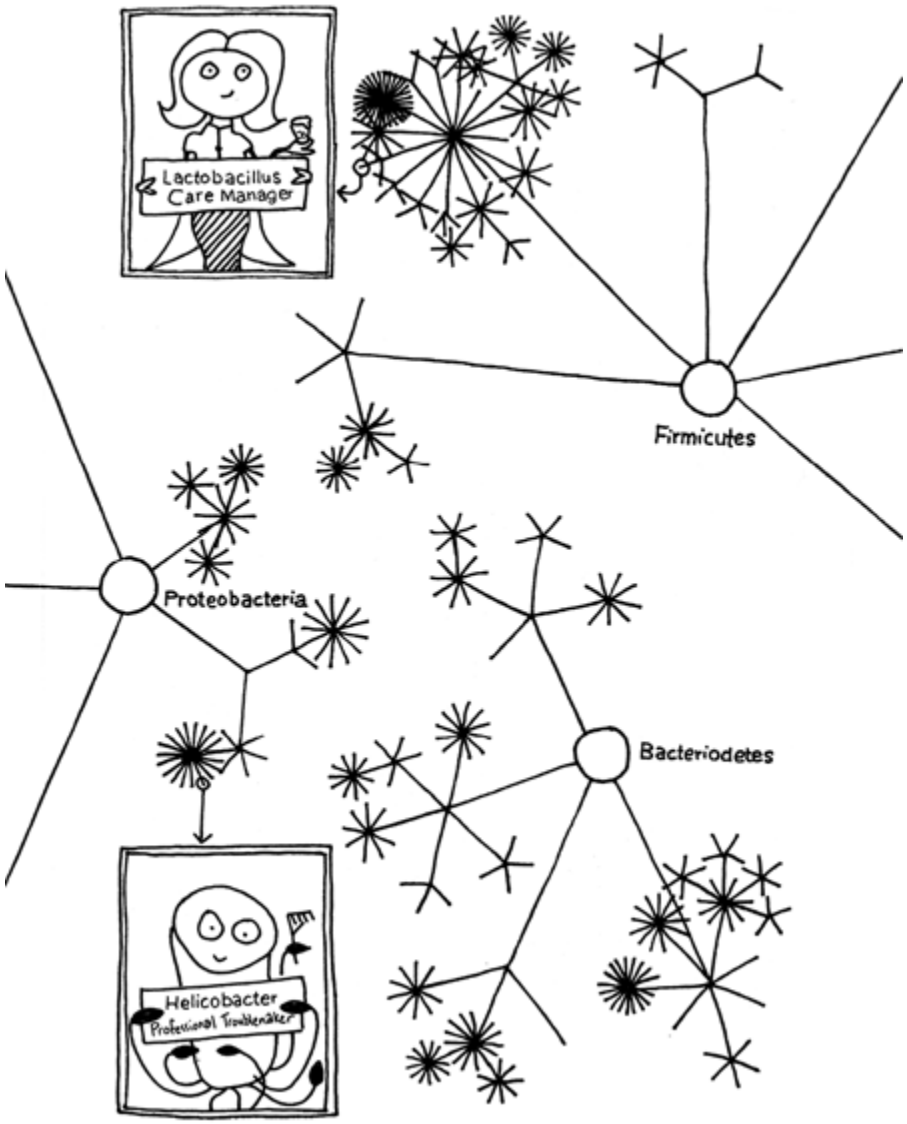
For those unfamiliar with the term *opisthokont* (it comes from the Greek words for "rear" and "pole"), it describes the group that includes all animals —humans as well—and also fungi. So, the next time you meet an ant in the street you can give it a friendly wave as a fellow opisthokont. The most common eukaryotes found in the gut are yeasts, which are also opisthokonts. We are familiar with yeast as a rising agent for bread, but there are many other kinds.

Archaea are kind of in-betweeners. Not really eukaryotes, but not really bacteria, either. Their cells are small and complex. If this description seems a little vague, it may help if I say that the Archaea are pretty rad characters. They love the extreme things in life. Some are hyperthermophiles, which feel right at home in temperatures of more than 212 degrees Fahrenheit (100 degrees Celsius) and are often to be found hanging out near volcanoes. The acidophiles among the Archaea like to paddle around in highly concentrated acid. Barophiles (also called piezophiles) thrive under pressure and have specially adapted cell walls to allow them to live on the deep sea floor. Halophiles are at home in extremely salty water (they love the Dead

Sea). The rare characters among the Archaea that can be cultured in the lab are the cryophiles, which love the cold. They like laboratory freezers that keep them at a cozy minus 112 degrees Fahrenheit (minus 80 degrees Celsius). There is one species of Archaea often found in our gut that thrives on the waste products of other gut bacteria and can glow.

Returning to the main topic: bacteria make up more than 90 percent of the population of our gut. Biologists divide bacteria into more than twenty phyla or lineages. Members of different phyla are sometimes about as similar as human beings are to excavates (single-cell microbes with feeding grooves)—that is to say, not very. Most of the inhabitants of our gut belong to one of five phyla: mainly Bacteroidetes and Firmicutes, with a smattering of Actinobacteria, Proteobacteria, and Verrucomicrobia. These phyla are further divided into increasingly specific categories, until we eventually reach the level of the bacteria family. Members of a given family are relatively similar to each other. They eat the same food, keep similar company, and have similar abilities. Individual family members have impressive names like *Bacteroides uniformis*, *Lactobacillus acidophilus*, or *Helicobacter pylori*. The bacteria kingdom is huge.

Whenever scientists search humans for a particular bacterium, they constantly come across new, previously unknown species. Or they discover known species in unexpected places. In 2011, a group of researchers in the United States decided to examine the flora of volunteers' belly buttons, just for fun. One subject's navel was found to contain bacteria that were previously known to live only in the seas off the coast of Japan—despite the fact that the volunteer had never even been to Asia. Globalization is not just your local corner shop turning into a McDonald's—it affects even the contents of our navels. Every day, billions and billions of foreign microorganisms fly round the world without paying a single cent for their tickets.



Rough overview of the three most important phyla of bacteria and their subgroups. Lactobacilli *are Firmicutes, for example.*

Everyone has their own personal collection of bacteria. It could even be described as a unique bacterial fingerprint. If you were to take swabs from a dog and analyze the genes of its bacteria, the dog's owner could be easily identified with reasonable certainty. The same is true of computer keyboards. Anything we come into regular contact with carries our microbial signature. Everyone has some outlandish items in their collection that almost no one else will share.

The microbial landscape in our gut is just as unique and individual. So, how are doctors supposed to know what is beneficial and what is harmful? Uniqueness like this presents researchers with a problem. If they are trying to ascertain what influence our gut bacteria have on our health, it is no use finding out that Mr. Smith is carrying a strange Asian species and several other weird microbes in his gut. Scientists need to identify patterns to deduce facts from them.

So, since scientists are faced with more than a thousand different families of bacteria, they must decide whether they need to identify just rough lineages or whether they should look at every paid-up member of the *Bacteroides* bacteria family individually. *E. coli* and its evil twin EHEC are members of the same family, for example. The differences between them are infinitesimally small—but they are very tangible: *E. coli* is a harmless gut-dweller, while EHEC causes severe internal bleeding and diarrhea. It always makes sense to examine families or lineages when you want to know what damage individual bacteria can wreak.

The Genes of Our Bacteria

Genes are possibilities. Genes are information. Genes can be dominant, forcing features on us, or they can just offer their abilities for us to use or not. But most of all, genes are plans. They are incapable of doing anything unless they are read and implemented. Implementation of some of these plans is obligatory—they decide whether we are a human being or a bacterium, for example. Others (say, liver spots) can be left on the back burner for years and yet others might be carried for a lifetime without ever being expressed—for example, genes for large breasts. Some people might consider that a pity, others a blessing.

Taken together, our gut bacteria have 150 times more genes than a human being. This massive collection of genes is called a biome. If we could pick 150 different living things, parts of whose genetic blueprints we would like to possess, what would we choose? Some people might opt for the strength of a lion, the wings of a bird, the hearing of a bat, or the practical mobile home of a snail.

There are many reasons why it would be more practical to opt for bacterial genes instead. They can be taken in easily via the mouth, unfurl their abilities in the gut, and even adapt to our lifestyle. Nobody needs a snail's mobile home all the time, and no one needs breast-milk-digestion helpers forever. The latter disappear gradually after weaning. It is not yet possible to examine all the genes of our gut bacteria at once. However, it is possible to search specifically for individual genes, if you know what you are looking for. We know that babies contain more active genes for digesting breast milk than adults do. The guts of obese people are often found to contain more bacterial genes involved in breaking down carbohydrates. Older people have fewer bacterial genes for dealing with stress. In Tokyo, gut bacteria can help digest seaweed, and in Toronto, they probably can't. Our gut bacteria paint a rough portrait of who we are: young, chubby, or Asian, perhaps.

The genes of our gut bacteria also inform us about our body's abilities. The pain-relief drug acetaminophen can be more toxic for some people than others: some gut bacteria produce a substance that influences the liver's ability to detoxify the drug. Whether you can pop a pill to cure your headache without a second thought is decided partially in your gut.

Similar caution should be exercised with general dietary tips. Soy's ability to protect against prostate cancer, cardio-vascular disease, or bone disorders, for example, has now been proven. More than 50 percent of Asians benefit from this effect. Among people of European heritage, the beneficial effect is found among only 25 to 30 percent of the population. This cannot simply be explained by human genetic differences. The difference is due to certain bacteria. They are found more commonly in the guts of Asians, where they are able to coax the health-promoting essence out of tofu and other soy products.

It is great for science when it identifies the individual bacterial genes that are responsible for this beneficial effect. In such cases, science can be said to have come up with an answer to the question of how gut bacteria influence our health. But we want more than that. We want to understand the big picture. If you look at all the bacterial genes so far discovered, the small individual groups of genes responsible for breaking down painkillers or soy products fade into the background. The common features they share

dominate the picture. Every microbe contains many genes involved in breaking down carbohydrates or proteins and in producing vitamins.

Science has the same problem when investigating the microbiome that the Google generation regularly faces. We ask a question and six million sources send us simultaneous answers. We don't respond by telling them to form an orderly line. We have to sort them shrewdly into categories, weed out the irrelevant ones, and recognize important patterns. One important step in this direction was the discovery of the three human enterotypes in 2011.

Researchers in Heidelberg, Germany, were using cutting-edge technology to investigate the human gut biome. They expected to see the usual picture: a chaotic mixture of many different bacteria, including a host of unknown species. What they actually discovered came as a surprise. Despite the great diversity, there was order. One of three families was always dominant in the realm of bacteria. Suddenly, the whole mess of more than a thousand families looked much more organized.

The Three Gut Types

A person's enterotype depends on the family of bacteria that dominates the microbe population of their gut. The choice is between families that bask in the glory of the names *Bacteroides*, *Prevotella*, and *Ruminococcus.* Researchers identified these enterotypes distributed among Asians, Americans, and Europeans, irrespective of age or gender. In the future, enterotyping may help doctors predict a whole range of characteristics, such as the body's response to soy, nerve resilience, or susceptibility to certain diseases.

Practitioners of traditional Chinese medicine who were visiting the institute in Heidelberg at the time of this discovery recognized an opportunity to combine their ancient knowledge with modern medicine. Classical Chinese medical theory has always divided people into three groups according to how they react to certain medicinal plants, such as ginger. The families of bacteria in our bodies also have different characteristics. They break down food in different ways, produce different

substances, and detoxify certain toxins but not others. Furthermore, they may also influence the gut flora by either encouraging or attacking bacteria from the other two groups.

Bacteroides

Bacteroides are the best-known family of gut bacteria and often form the dominant population. They are experts in breaking down carbohydrates, and they possess a huge collection of genetic blueprints, which allows them to manufacture any enzyme they need to accomplish that task. Whether we eat a steak, munch a large salad, or chew on a raffia doormat in a drunken stupor, *Bacteroides* know straight away which enzymes they need. They are equipped to extract energy from whatever we ingest.

Their ability to extract the maximum energy from everything and pass it on to us has led to the suspicion that they may be responsible for an increased tendency to gain weight. Indeed, *Bacteroides* do seem to like meat and saturated fatty acids. They are more common in the guts of people who eat plenty of sausages and the like. But, does having them in our gut make us fat, or does being fat lead to having them in our gut? This question remains to be answered. *Bacteroides* carriers are also likely to have a weakness for their colleagues, *Parabacteroides.* These bacteria are also particularly deft at passing on as many calories to us as possible.

This enterotype is also notable, among other things, for its ability to produce particularly large amounts of biotin. Other terms for biotin include vitamin B7 and vitamin H. It was given the name vitamin H in the 1930s because of its ability to heal a certain skin condition caused by consuming too much raw egg white. “H is for healing” might not be the most creative mnemonic, but it is a useful one nonetheless.

Vitamin H neutralizes avidin, a toxin found in raw eggs. It causes the skin disease in question by binding strongly with vitamin H, leaving the body deficient in that substance. So, eating raw eggs causes vitamin H deficiency, which in turn can lead to skin disease.

I do not know who was eating enough raw eggs in the 1930s to lead to the discovery of this connection. I do, however, know who might possibly end up eating so much avidin in the future that they could have problems with vitamin H—pigs who accidently roam into a field of genetically modified corn. Genetic engineers have created transgenic corn with a gene

that produces avidin to make it less susceptible to insect damage during storage. When pests—or stray pigs—consume the corn, they are poisoned. When the corn is cooked, it is no longer toxic, just like a good hard-boiled egg.

Another indication that our gut microbes produce vitamin H is the fact that some people excrete more of it than they take in. Since no human cell is capable of producing this substance, the only possible explanation for this is that our bacteria are functioning as hidden vitamin H factories. Vitamin H is not only necessary for "healthy-looking skin, shiny hair, and strong nails," as you might read on the packages of supplements you can buy in your local pharmacy. Biotin is also involved in some of the body's vital metabolic processes. We need it to synthesize carbohydrates and fats for our body, and to break down proteins.

Skin, hair, and nail problems are not the only effects of biotin deficiency. It can also cause depression, lethargy, susceptibility to infections, neurological disorders, and increased cholesterol levels in the blood. However, let me issue a serious WARNING here: the list of symptoms caused by any vitamin deficiency is formidable. Most people reading them feel the symptoms apply to them in some way. But it is important to remember that you can catch a cold or feel a bit lethargic without jumping to the conclusion that you have a biotin deficiency. And cholesterol levels are more likely to be raised by eating a big plate of bacon for breakfast than by eating the avidin in an undercooked egg.

However, some people in higher-risk groups may well consider the possibility of a biotin deficiency. That includes anyone who takes antibiotics for an extended period, heavy drinkers, anyone who has had part of their small intestine removed, anyone reliant on dialysis, and people on certain kinds of medication. These people require more biotin than they can get from a normal diet. One healthy higher-risk group is pregnant women: developing babies use up biotin like aging refrigerators gobble up electricity.

So far, no scientific studies have been carried out to investigate how much biotin our gut bacteria provide us with. We know that they produce some, and that antibacterial medications such as antibiotics can cause biotin deficiency. Investigating whether members of the *Prevotella* enterotype are more likely to suffer from a biotin deficiency than someone of the

Bacteroides enterotype would be a pretty exciting research project. But, since the existence of the three different enterotypes was only discovered in 2011, there are many more pressing questions we need to answer.

It is not only their good output that makes *Bacteroides* so successful; they also work hand in hand with others. Some species in the gut make a living by clearing away the waste left by *Bacteroides.* This is a win-win situation: *Bacteroides* work better in tidy surroundings, and the waste-disposal organisms have a secure source of income. On a different level, we find the composters. These organisms not only utilize waste products for their own ends, they also use them to make products that *Bacteroides* can use in turn. For some metabolic pathways, *Bacteroides* themselves take on the role of composter. For example, if they need a carbon atom to modify a molecule, they simply reach up and grab it out of the atmosphere in the gut. They always find what they are looking for, since carbon is a waste product of our metabolism.

Prevotella

In many ways, the *Prevotella* family is the opposite of *Bacteroides.* Studies have shown that they are more common in the guts of vegetarians, but they also appear in moderate meat eaters and in convinced carnivores. Our diet is not the only factor that influences the colonization of our gut. But more about that presently.

Prevotella also have a group of bacterial colleagues they prefer working with—*Desulfovibrionales*. *Desulfovibrionales* often have a long flagellum —a whiplike tail used to propel them along—and so, like *Prevotella*, they are adept at trawling through our mucus membranes looking for useful proteins. They then either eat those proteins or use them to build who-knows-what. *Prevotella* produce sulfur compounds when they work. The smell of these compounds is familiar, as we know it from boiled eggs. If it weren't for *Desulfovibrionales* whipping around with their propeller-tails, snapping up the sulfur, *Prevotella* would soon find themselves drowning in a sulfur swamp of their own making. Incidentally, this gas is not dangerous to human health. Our nose wrinkles at it as a precautionary measure as it can slowly become toxic as concentrations increase a thousandfold.

Another substance that contains sulfur and has an interesting smell is the vitamin associated with this enterotype: thiamine. Also known as vitamin

B1, this is one of the most widely recognized and important vitamins. Our brains require it not only to keep the nerves well nourished, but also to coat them in an electrically insulating layer of fat. This explains why a thiamine deficiency may be the cause of muscle tremors and forgetfulness.

A very serious lack of vitamin B1 causes a disease called beriberi. It was described in Asia as early as AD 500. Beriberi means “I cannot, I cannot” in the Sinhalese language of Sri Lanka and refers to the fact that sufferers have difficulty walking due to nerve damage and muscle atrophy. It is now known that polishing rice removes the vitamin B1 it contains, and a diet made up predominantly of this kind of rice leads to an onset of symptoms within a few weeks.

While not resulting in serious neurological or memory disorders, a less severe vitamin B1 deficiency can cause irritability, frequent headaches, and lack of concentration. More advanced cases can cause a susceptibility to edema and heart problems. But once again, beware: these symptoms can have many causes. They are only a reason for concern when they are unusually frequent or severe. They are rarely caused exclusively by a vitamin deficiency.

Studying the symptoms of vitamin deficiencies provides a useful insight into the part played by vitamins in certain processes. Anyone whose diet does not consist exclusively of polished white rice or alcohol is usually well supplied. The fact that our gut bacteria help supply us with essential vitamins means they are far more than just a load of flagellating sulfur-poopers—and that is what makes them so fascinating.

Ruminococcus

Opinions are divided on this family—scientific opinions, at any rate. Some scientists who decided to investigate the existence of enterotypes for themselves found *Prevotella* and *Bacteroides*, but no *Ruminococcus* group. Others swear this third group exists, and yet others insist there is even a fourth or fifth group, or more. Such a state of affairs can really ruin the coffee break at a medical congress.

Let’s agree for the sake of argument that there is at least a possibility that this group exists. Its proposed favorite food is the cell walls of plants. Possible colleagues include *Akkermansia* bacteria, which break down the mucins in mucus and absorb sugar pretty quickly. *Ruminococcus* produces a

substance called haem, which the body needs for many things, including producing blood.

One character who probably had problems producing haem was Count Dracula. A genetic defect has been identified in his home country, Romania, that results in symptoms that include a lack of tolerance to garlic, sensitivity to sunlight, and the production of red urine. This urine discoloration is caused by a defect in blood production that means sufferers excrete the unfinished precursors of blood production. Nowadays, those affected by the condition—called porphyria—are given medical treatment rather than the starring role in a horror story.

Even if the *Ruminococcus* enterotype does not exist, there is no doubt that these bacteria are present in our gut. So, it is useful that we now know more about them—and about Dracula and red pee. Our bacteria-free laboratory mice have trouble forming haem, and so it stands to reason that bacteria are somehow important in this process.

Now we are more familiar with the tiny world of the microbes in our gut. Their genes represent a huge pool of borrowed abilities. They help us digest our food, and they produce vitamins and other useful substances. We are just beginning to recognize enterotype commonalities and search for patterns. And we do this for one reason: 100 trillion tiny creatures reside in our gut and that cannot but have an effect on us. So, let’s now go one step further and explore the palpable effects they have on us. Let’s take a closer look at how these gut bacteria affect our metabolism, and examine which ones do us good and which ones do us harm.

The Role of the Gut Flora

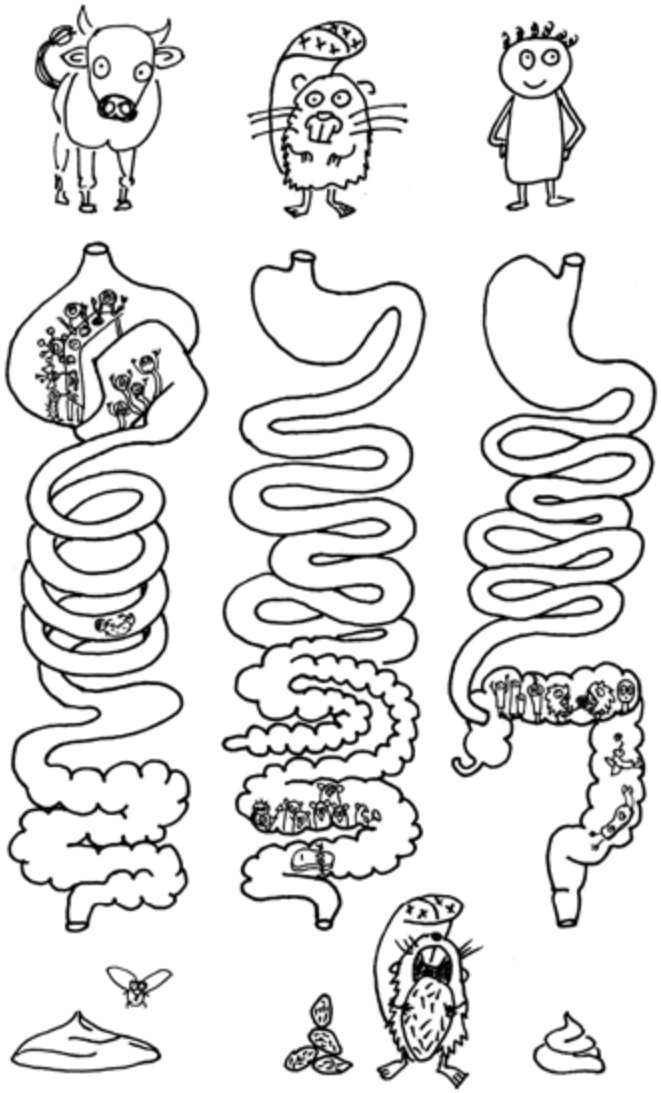
SOMETIMES WE TELL fibs to our children. We do it because these little untruths are so nice. There's the one about the man with the big white beard who arrives once a year on his tuned-up reindeer sleigh piled high with children's presents, or the one about the Easter bunny hiding chocolate eggs in the garden. Sometimes, we don't even realize when we are not telling the truth—like when we encourage a toddler to eat up: "One spoon for Daddy, one spoon for Mummy, one for Granny, and one for Granddad..." If we wanted to encourage Junior in a scientifically correct way, we would have to say, "One spoon for you, baby. A small part of the next spoon for your *Bacteroides* bacteria. An equally small part for your *Prevotella.* And a teeny-weeny bit for a few other microorganisms waiting in your tummy to be fed." We might well send a friendly vote of thanks down to the micro-colleagues enjoying the meal in baby's belly. After all, *Bacteroides* and company work hard to help keep baby well fed. And not only in infancy. Adults, too, receive nutrition back from their bacterial gut-dwellers, morsel by morsel. Gut bacteria process food that we cannot break down unaided and share the results with us.

The idea that the bacteria in our gut might influence our overall metabolism, and therefore our weight, is only a couple of years old. The basic concept is that bacteria do not steal anything from us when they share our food in this way. Very few gut bacteria reside in the small intestine, where we break down our food for ourselves and absorb the nutrients from it. The highest concentration of bacteria is found where the digestive process is almost finished and all that remains is for the undigested remnants to be transported away. The farther you travel from the small intestine toward the final exit from the gut, the more bacteria you will find per square inch of gut membrane. It is our gut that makes sure this remains so. If the equilibrium is disturbed and large numbers of overconfident bacteria migrate to the small intestine, we have a case of what doctors call bacterial overgrowth. This relatively unexplored condition causes

symptoms that can include severe bloating, abdominal pain, joint pain, and gastrointestinal infections, as well as nutrient deficiencies and anemia.

In ruminants such as cows, this construction design is reversed. These large animals pride themselves on their ability to survive by eating only grass and a few other plants. No other animal on the farm would make fun of them for being puny vegans, so what is their secret? Cows keep their bacteria right at the top of their digestive tract. They don't even bother trying to digest their food themselves first, but pass the complex plant carbohydrates straight on to *Bacteroides* and company. Their microbes turn these carbohydrates into an easily digested feast for the cow.

It can be practical to keep your bacteria so close to the beginning of your digestive tract. Bacteria are rich in protein—so, from a food point of view, they are tiny little steaks. When they have finished their life's work in the cow's stomach, they slip farther down the system, where they are digested. They are a large source of protein for the cow—tiny microbial tenderloins, bred by themselves. Our bacteria are too far down the system to provide this practical steakhouse service so we pass them out of our gut undigested.



Rodents keep their microbes as far down the system as we do, but are more loath to waste the bacterial protein they contain. Their simple solution is to eat their own feces. We don’t do that, preferring to buy meat or tofu at the supermarket to compensate for the fact that we are unable to process protein-rich bacteria in our large intestine. However, we still benefit from the work of our bacteria, even if we don’t digest them. Bacteria produce nutrients that are so tiny we can absorb them directly into the cells of our gut.

Bacteria can also perform this service outside the gut. Yogurt is nothing other than milk that has been predigested by bacteria. Much of the sugar in the milk (lactose) has already been broken down and transformed into lactic

acid (lactate) and smaller sugar molecules. That is why yogurt is both sweeter and sourer than milk. The newly formed acid has another effect on the milk. It causes the milk protein to curdle, giving the yogurt its characteristic thick consistency. Predigested milk (yogurt) saves our body some work—we just have to finish off what the bacteria started.

It is an especially good idea to employ those bacteria to predigest our food that manufacture healthy end products. Mindful yogurt manufacturers often use bacteria that produce more dextrorotatory (right-turning) than levorotatory (left-turning) lactic acids. Molecules of the two kinds of lactic acid are mirror images of each other. Feeding the human digestive system with levorotatory lactic acid molecules is like giving a left-handed pair of scissors to a right-handed person: they're hard to handle. That is why it is a good idea to pick yogurt from the supermarket shelves that states on the container: "Contains mainly dextrorotatory [or right-turning] lactic acid."

Bacteria do more than just break down our food. They also produce completely new substances. Fresh cabbage, for example, is less rich in vitamins than the sauerkraut it can be turned into—those extra vitamins are made by bacteria. Bacteria and fungi are responsible for the taste, creamy consistency of, and holes in cheese. Bologna sausage and salami are often made with starter cultures—that's butchers' code for "We daren't tell it you straight, but it is the bacteria (mainly *Staphylococcus*) that make it so tasty." Lovers of wine or vodka appreciate the metabolic end product of yeasts—known as alcohol. The work of these microorganisms does not end in the wine barrel. Almost none of what a wine taster will tell you is actually to be found in the bottle. The wine's bouquet, for example, develops so late because bacteria need time to do their work. They sit in waiting at the back of the tongue, where the process of transforming what we eat or drink begins. The substances they release during that process create the aftertaste so appreciated by the wine lover. And each connoisseur will experience a slightly different taste depending on the population of bacteria on their tongue. Still, it's nice to get such an enthusiastic reaction to the presence of these much-maligned microbes.

The bacteria population of our mouth is only about one-ten-thousandth of the number that live in the gut, yet we still taste the results of their work. Our digestive tract should be grateful for the fact that it has such a large population with such a wide range of skills. While simple glucose and

fructose are easily digested, many people's guts start to flag when it comes to lactose, the sugar contained in milk. Their owners then suffer from a lactose intolerance. Complex plant carbohydrates would flummox a gut if it were expected to have at the ready every enzyme needed to break them down. Our microbes are experts in dealing with these substances. We provide them with somewhere to live and the undigested remains of our food—and they keep busy dealing with the stuff that's too complicated for us to do.

In the industrialized world, about 90 percent of our nutrition comes from what we eat, and we are fed about 10 percent by our bacteria. So, after nine lunches, meal number ten is on the house, so to speak. Feeding adults is the main occupation of some of our bacteria. That does not mean that it makes no difference what we eat—far from it. And the kind of bacteria that are feeding us also makes a big difference. In other words, if we are concerned about our weight, we need to think about more than just the big, fat calories we consume and remember that our bacteria are at the dinner table with us.

How Might Bacteria Make Us Fat? Three Theories

1. "Chubby" Bacteria

The gut flora might include too many bacteria that program a person for chubbiness. These chubbiness-inducing bacteria are efficient at breaking down carbohydrates. If the number of chubby bacteria gets out of hand, we have a problem. Skinny mice excrete a certain quantity of indigestible calories while their overweight peers excrete significantly fewer. The chubby bacteria in the latter group extract every last smidgen of energy from the same amount of food and cheerfully feed it to Mr. or Ms. Mouse. For humans, that can mean some people pile on the pounds even though they eat no more than others. It could be that their gut flora is extracting more energy from the food they eat.

How can that be possible? Bacteria are able to make various fatty acids out of indigestible carbohydrates. Vegetable-loving bacteria tend to manufacture fatty acids for the gut and the liver, and others produce fatty acids that feed the rest of the body. A banana is less likely to make you fat

than half a chocolate bar containing the same number of calories. That is because plant carbohydrates are more likely to attract the attention of bacteria that provide fatty acids to local customers like the liver. The chocolate bar, on the other hand, is more likely to attract the attention of the full-body feeders.

Studies carried out on obese subjects show that they have less overall diversity in their gut flora and that certain groups of bacteria prevail—primarily those that metabolize carbohydrates. To succeed in becoming obese, however, a few other conditions must be met. Experiments with laboratory mice showed that some weighed 60 percent more at the end of the trial than at the beginning. Full-body-feeding bacteria cannot cause so much weight gain alone. This prompted scientists to consider another marker for extreme weight gain: inflammation.

2. Inflammation

Patients who have metabolic problems, such as obesity, diabetes, and high blood-lipid levels, usually have slightly increased levels of infection markers in their blood, too. These infections are not so high that they require treatment, as they would, say, if they were caused by an infected wound or septicemia. That’s why doctors call these subclinical infections. If there is anyone who knows a thing or two about infection, it’s bacteria. They have a signaling substance on their surface that tells the body when to get infected.

When we get injured, this reaction is useful. Infection reactions flush out bacteria or attack them. As long as bacteria remain in their cozy mucus-membrane home in the gut, this signaling substance goes unnoticed. But when bacteria appear in disadvantageous combinations, or when their host eats an overly fatty diet, too many of them can find their way into the bloodstream. The body then slips into low-key infection mode. From the evolutionary point of view, it’s worth paying that price to build up fat reserves for leaner times.

Bacterial-signaling substances can also latch onto other organs and affect metabolism from there. In rodents and humans, they dock onto the liver or the fatty tissue itself and encourage the deposition of more fat. They also have an interesting effect on the thyroid gland. Bacterial infections hinder

its function, causing it to produce fewer thyroid hormones, slowing the rate at which the body burns fat.

Unlike acute infections, which cause weight loss or even emaciation, subclinical infection causes weight gain. Bacteria are not the only possible cause of subclinical infections—hormone imbalances, too much estrogen, lack of vitamin D, or too much gluten-rich food have all been observed to have a similar effect.

3. Cravings

Now, brace yourself for a crazy idea! A hypothesis postulated in 2013 suggests that gut bacteria can affect their host's appetite. Roughly speaking, the theory is that late-night cravings for chocolate-covered toffees followed by an entire bag of party pretzels do not originate in the organ that calculates our tax returns. Not our brains but our guts are the home of gangs of bacteria that crave hamburgers after three days on a diet. Somehow they manage to pass on that message in a very persuasive way, because we find it almost impossible to deny them any wish.

To understand this hypothesis, we have to try to get our head around the issue of food. Faced with the choice between two different dishes, we make the decision based on what we happen to fancy at that moment. The amount of our chosen dish that we actually eat is controlled by the feeling of satiety. In theory, bacteria have ways and means of influencing both those things. Again, we can currently only conjecture that they also have a say in our appetite. But in evolutionary terms, it is not such a silly idea. What and how much we eat can be a matter of life and death for them. In three million years of coevolution, even simple bacteria have had time to adapt optimally to life with their human hosts.

If you want to trigger a craving for specific foods, you have to gain access to the brain. That is no mean feat. The brain is wrapped in a sturdy membrane called the meninges. Even more impenetrable than the meninges are the coats that surround all the blood vessels passing through the brain. The only things that can make it through this tangled mess are pure sugar, minerals, and anything that is as small and fat-soluble as a neural transmitter. Nicotine, for example, makes it through to the brain, where it triggers reward signals or a feeling of relaxed alertness.

Bacteria can produce particles that are small enough to make it through the coating of the blood vessels into the brain. Examples include tyrosine and tryptophan. These two amino acids are converted into dopamine and serotonin in the cells of the brain. Dopamine? Wasn't that famously associated with the brain's reward system? And serotonin? That sounds familiar, too, doesn't it? Lack of it causes depression. It can make us feel contented and sleepy. Just think about last year's Christmas dinner. Did you end up dozing on the couch after enjoying it, feeling lethargic and sleepy but also contented?

So the theory is this: our bacteria reward us when we send them a decent delivery of food. It feels pleasant and whets our appetite for the next meal. They do this not only directly by means of the substances they produce, but also by cranking up the body's production of certain transmitters. The same principle applies to the feeling of satiety.

Several studies have shown our satiety signal transmitters increase considerably when we eat the food our bacteria prefer. What our bacteria prefer is food that reaches the large intestine undigested, where they can then gobble it up. Surprisingly enough, those foods do not include pasta and white bread ;-). For more on this, turn to the section on prebiotics in the last chapter of this book.

The feeling of satiety generally comes from two sides: from the brain and from the rest of the body. A lot can go wrong here. In obese people, the gene that codes for satiety can be defective, and such people simply do not get that full feeling after eating. According to the selfish brain theory, the brain does not receive enough of the energy eaten as food and so decides that it is still hungry. But it is not only our body tissue and our gray matter that depend on the food we eat—our microbes also need to be fed. They may seem small and insignificant by comparison with our body size—accounting for just 4½ pounds (2 kilos) of our body weight. So what right do they have to butt in?

When we consider the range of functions carried out by our gut flora, it is not surprising that these microbes are also able to express their wishes. They are, after all, the immune system's most important trainers, digestion assistants, producers of vitamins, and experts in detoxifying moldy bread or medical drugs. The list is actually much longer, of course, but the message

should be clear: they should be able to have a say in whether we feel full after eating.

We do not yet know whether different bacteria express different desires. When we give up sweets, we eventually stop missing them so badly at some point. Is that because the gummy bear and chocolate lobby has been starved out? We can only speculate.

The important thing is not to reduce the human body to a two-dimensional cause-and-effect machine. The brain, the rest of the body, bacteria, and the elements in our food all interact with each other in four dimensions. Striving to understand all these axes is surely the best way to improve our knowledge. However, we can more easily tinker with bacteria than with our brain or our genes—and that is what makes microbes so fascinating. The nutrition we receive from our bacteria is not only important for fighting the flab, it also affects the levels of fats such as cholesterol in our blood. This realization could be quite highly charged as obesity and high cholesterol levels are closely connected with the greatest health issues of our time: hypertension, arteriosclerosis, and diabetes.

Cholesterol and Gut Bacteria

The connection between bacteria and cholesterol was first discovered in the 1970s. American scientists studying Maasai warriors in Africa had been surprised to find the levels of cholesterol in their blood were low, despite a diet consisting almost entirely of meat and milk. This excessive amount of animal fat did not cause high blood-lipid levels. The scientists suspected a mysterious substance in the milk they drank might be causing their cholesterol levels to remain low.

The scientists then set about doing all they could to find that mysterious ingredient. They tested cow’s milk and camel’s milk and even rat’s milk. Sometimes they managed to reduce cholesterol levels, sometimes not. These results told the scientists nothing. In another experiment, they gave the Maasai warriors a vegetable-based milk replacement product (Coffee-mate®) with high levels of cholesterol added to it. Still, the subjects’ blood

cholesterol levels did not rise. The scientists saw that their theory about a mysterious milk component was disproven.

They had meticulously noted that the Maasai often drank curdled milk, but no one considered the fact that certain bacteria are required to curdle milk. That would have explained the results of their Coffee-mate® experiment. Bacteria that have already settled in the gut can continue to live there even when milk is replaced with plant-based creamer enriched with cholesterol. Even when the Maasai's cholesterol levels were seen to sink by 18 percent whenever they drank curdled milk rather than fresh milk, scientists continued to search for the mysterious milk substance—blind dedication that brought no results.

These studies of the Maasai would not live up to modern scientific expectations. The test groups were too small, and the Maasai spend about thirteen hours a day walking and one month a year fasting. They simply cannot be compared to meat-eating Westerners. However, the results of these studies were rediscovered decades later by researchers who were now aware of the importance of bacteria. Cholesterol-lowering bacteria? Why not test that in the lab? Take a flask of nutrient broth warmed to a balmy 98.6 degrees Fahrenheit (37 degrees Celsius), add cholesterol and some bacteria—et voilà! The bacterium they used was *Lactobacillus fermentus*, and the cholesterol they had added was... gone! At least a considerable proportion of it was.

Experiments can have very different results, depending whether they are carried out in glass flasks or inside opistho-konts. It's like an emotional rollercoaster ride for me when I read in scientific papers sentences like "The bacterium *L. plantarum* Lp91 can significantly lower high cholesterol and other blood lipid levels, increase good HDL cholesterol, and lead to significantly lower rates of arteriosclerosis, *as could be shown in 112 Syrian golden hamsters*." I have never been so disappointed by Syrian golden hamsters. Experiments on animals are a good way to begin tests on living systems, but if the sentence had ended "as could be shown in 112 obese Americans," the whole thing would be a lot more impressive.

But a result like that can still be worth a lot. Studies on mice, rats, and pigs yielded such promising results for some bacteria that scientists considered it reasonable to begin human testing. The subjects were regularly administered certain bacteria and after a period of time their

cholesterol levels were measured. The bacteria species, the quantities, the duration, and the way they were administered were all varied. Some results were positive and others were not. Also, no one really knew whether sufficient numbers of the administered bacteria even survived their bath in the acid juices of the stomach long enough to have an effect on blood cholesterol levels.

Really valuable studies began about twenty years ago. For one experiment in 2011, 114 Canadians ate specially produced yogurt twice a day. The bacterium added to the yogurt was *Lactobacillus reuteri*—in a form particularly resistant to digestion. Within six weeks, their levels of bad LDL cholesterol sank by 8.91 percent. That's about half the improvement attained by taking a mild anti-cholesterol drug—but without the side effects. Studies using other types of bacteria lowered cholesterol levels by as much as 11 to 30 percent. Follow-up research still needs to be carried out to verify these promising indications.

There are several hundred bacteria candidates that might be tested in future. To sift out the less likely ones, we have to ask the following kinds of questions. What abilities does such a bacterium need to have? Or rather, "What genes does it need to have?" The most likely candidates we know of today are BSH genes. BSH stands for bile salt hydrolase. Bacteria with these genes can convert bile salts. But what do bile salts have to do with cholesterol? The answer is in the name. Cholesterol comes from the Greek words *chole* (bile) and *stereos* (solid). Cholesterol was first discovered in gall stones. Bile, which is stored in the gall bladder, is the body's transport medium for fats and cholesterol. BSH allows bacteria to alter bile to make it work less efficiently. The cholesterol and fat dissolved in bile can then no longer be absorbed by the body and they end up, to put it bluntly, down the toilet. This mechanism is useful for bacteria because it weakens the effect of bile, which can attack their cell membranes. This protects the bacteria on their long journey to their final destination—the large intestine. Bacteria also have a few other mechanisms for dealing with cholesterol: they can absorb it directly and incorporate it in their cell walls, they can convert it into a new substance, or they can manipulate organs that produce cholesterol. Most cholesterol is produced in the liver and the gut, where tiny messenger substances manufactured by the bacteria can partly control those processes.

But we need to take a step back and ask cautiously: does the body always want to get rid of its cholesterol? It produces between 75 and 90 percent of our cholesterol itself. And that takes a lot of work! One-sided media reporting has given cholesterol a bad name, making people believe it is only evil. That is quite wrong. *Too much* cholesterol is not such a good thing, but neither is *too little*. If it weren't for cholesterol, we would have unstable cells and no sex hormones or vitamin D. Fat and cholesterol are not only an issue for Granny and her weakness for cream cakes or sausages. They are an issue for every one of us. Studies have shown a connection between too little cholesterol and memory problems, depression, and aggressive behavior.

Cholesterol is also the miraculous base material for building all sorts of structures. Too much of it is indeed harmful—it's all about finding the right balance. Our bacteria would not be our bacteria if they didn't have the ability to help us achieve that. Some bacteria produce more of a substance called propionate, which inhibits the production of cholesterol. Others produce more acetate, which promotes the production of cholesterol.

Who would have thought it? A chapter that began with bright, little spots of bacteria ending with concepts like appetite and satiety or substances like cholesterol? To summarize: Bacteria help to feed us, make some foods more digestible, and produce their own substances. Some scientists now support the theory that our gut microbiota can be considered an organ. Just like the other organs in our body, this organ has an origin, develops along with us, is made up of a load of cells, and is in constant contact with its fellow organs.

The Bad Guys—Harmful Bacteria and Parasites

THERE ARE GOOD guys and there are bad guys in the world—and the same goes for the world of our microbes. One thing unites most of the bad guys: they only want what's best... for themselves.

Salmonellae in Hats

Even the most courageous of cooks sometimes feel a pang of primal fear while beating eggs—fear of the raw threat posed by *Salmonella*! Everyone knows someone who has endured devastating diarrhea and venomous vomiting after eating chicken that was not quite done or nibbling on a bit of raw cake mix.

Salmonella bacteria can get into our food in unexpected ways. Sometimes, globalization helps them find a home in our chicken, meat, or eggs. This is how it can happen in Germany, where I live. The cheapest source of feed grain for chickens is Africa. So, we fly it in to feed the fowl in our poultry farms. However, there are more wild tortoises and lizards wandering around in Africa than Germany. *Salmonella* bacteria travel to our climes along with the chicken feed. How so? Well, they are part of the normal gut flora of reptiles. While the African farmer is working in the fields, a tortoise might merrily be doing its business in a sack of grain destined for Germany. After an exciting flight with a wonderful view over the clouds, the grain, along with its stowaway tortoise-poop bacteria, ends up in a German poultry farm, where it is eaten by a hungry chicken. *Salmonella* bacteria are not part of a chicken's natural gut flora, but they are a common pathogen. Similar contamination can occur in other countries when animal feed contains materials where *Salmonellae* may lurk.

Once inside the bird's gut, the *Salmonellae* can multiply, and they are eventually excreted. Since chickens have only one hole for all export goods, the egg cannot avoid coming into contact with *Salmonellae* in the bird's

feces. The bacteria are then found only on the shells of eggs—they only get inside when the shell is cracked.

But what about *Salmonellae* in chicken meat? How do they get there? That's a rather unsavory story. Cheaply fed chickens are usually sent to large industrial slaughterhouses to meet their maker. Once they have been slaughtered and beheaded, they are dunked in huge tanks of water. Those tanks are like a wellness spa for *Salmonella* bacteria, complete with a colonic irrigation service for the chickens. In a slaughterhouse dispatching 200,000 birds a day, one batch of cheap-feed chickens is enough to give the gift of *Salmonella* to all the other birds in the bath. The chickens then end up in the freezers of discount supermarkets. If they are roasted or grilled at high-enough temperatures, the *Salmonella* germs are soon killed off and can no longer cause problems for anyone.

Properly cooked meat is normally not the reason for most *Salmonella* infections. The problems begin when the frozen chicken is left to thaw in the kitchen sink or colander. Freezing and thawing does bacteria little harm. The huge library of bacteria in our laboratory includes germs, collected from patients, that easily survive temperatures of minus 112 degrees Fahrenheit (minus 80 degrees Celsius) and live merrily on when thawed. Heat is their nemesis. Even just ten minutes' exposure to a temperature of 167 degrees Fahrenheit (75 degrees Celsius) is enough to see off all *Salmonella* bacteria. That's why a carefully roasted chicken is not usually the culprit, but rather the lettuce leaves for the side salad, left to soak briefly in the same kitchen sink.

We come into regular contact with the gut flora of the livestock we keep, but we only notice it when they happen to include unfamiliar, diarrhea-causing bacteria. The rest is routine, so to speak, and after all, we have to get our bacteria from somewhere. Sticking to organic country eggs from chickens fed with home-grown grain is usually a reliable way to avoid dangerous bacteria—unless the farmer himself eats cheap chicken from a discount supermarket.

If our Sunday roast chicken is not roasted enough, we can end up eating not just chicken muscle cells but a few *Salmonella* cells, too. It takes between ten thousand and one million of these single-celled creatures to put us out of action. A million of these bacteria take up about one-fifth as much space as a grain of salt. So, how does an army of such tiny soldiers manage

to move a colossus like us—with the volume of about 600,000,000 grains of salt—inexorably toward the toilet? It's as if one hair of the American president's head were to rule over the entire population of the United States.

Salmonella bacteria double in number much more quickly than politicians' hairs—that's point one. As soon as the temperature rises above 50 degrees Fahrenheit (10 degrees Celsius), *Salmonellae* come out of hibernation and get busy breeding. They have delicate little arms that enable them to swim around until they find a place to attach to the gut. Once there, they invade our cells, which become infected and pump large quantities of fluid into the gut in an attempt to flush out the pathogen as quickly as possible.

It can take a few hours to a few days from accidental ingestion to watery flush-out. A self-induced colonic irrigation like this usually works well, unless the victim is too young, too old, or too frail. Antibiotics would do more harm than good here. Despite this natural cure, it is better for the gut to flatly refuse entry to *Salmonella,* however rude that may seem. After a visit to the toilet or a retching session into a sick bag, you should not take them by the hand and show them what life is like in the outside world. They should be given the cold shoulder by washing with very hot water and soap to let them know: it's not you, it's me—I just can't deal with your clinging personality.

Salmonellae are the most common type of bad guys we take in with our food. They are not found exclusively in poultry products, but poultry products are one of *Salmonellae*'s favorite hang-outs. *Salmonellae* come in several varieties. When we receive stool samples from patients at our laboratory, we can test them by exposing them to different antibodies. When an antibody bonds with the *Salmonellae,* they clump together into blobs that are big enough to see with the naked eye.

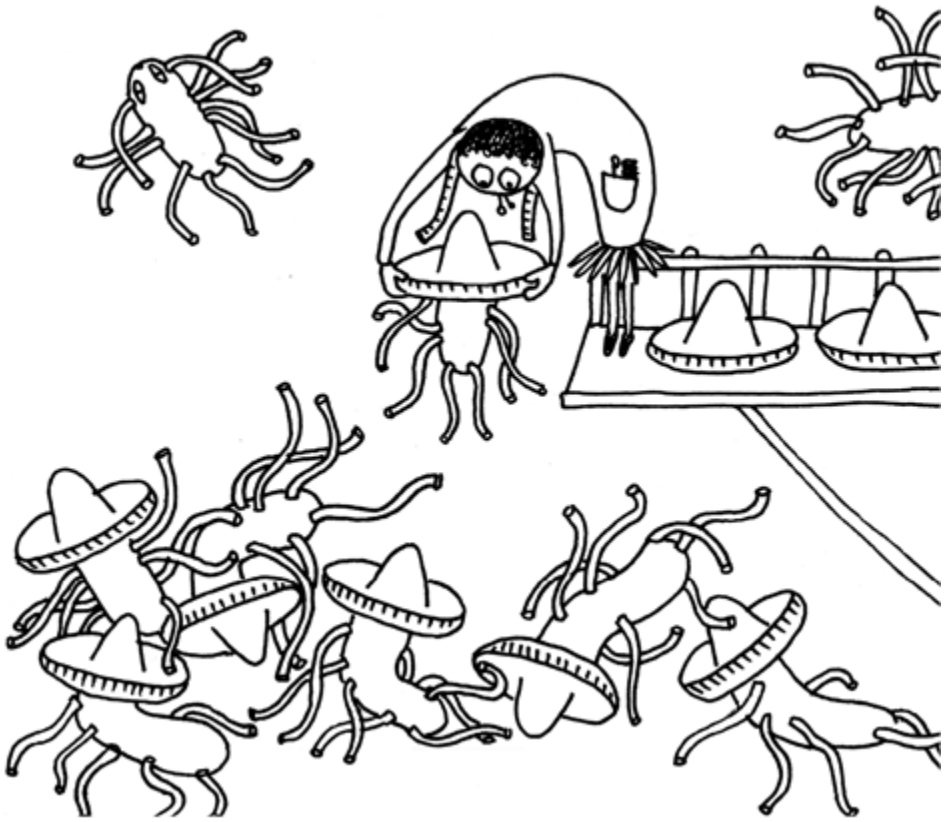
When that happens, we can say that the antibody to vomit-inducing *Salmonella* XY reacts strongly, so this must be vomit-inducing *Salmonella* XY. This is the same as the mechanism in our own body. Our immune system meets a couple of new *Salmonellae* and says, "Hmmm, I'm sure I must have a hat that fits them somewhere in my collection." It then rummages around in its wardrobes to find the right hat, adjusts it a little to create the perfect fit, then commissions a hatter to make headgear for a million *Salmonella* germs. When all the *Salmonella* bacteria are wearing

their new hats, they no longer look dangerous, but rather ridiculous. They are weighed down so much by the millinery that they are too heavy to swim around attacking anything. In this way, the test antibodies in the lab can be seen as a small selection of different hats. When the hat fits, the heavily sombreroed bacteria collapse into clumps and—depending on the hat—we can say which type of *Salmonella* was in the stool sample.

For those who do not necessarily want to send their immune system searching for hats and who are no great fans of diarrhea and vomiting, there are a few simple rules to follow.

Rule number one: Always use plastic chopping boards because they are easier to clean properly and provide fewer grooves and ridges for bacteria to hide in.

Rule number two: Always wash anything that comes into contact with raw meat or eggshells thoroughly with hot water—chopping boards, hands, cutlery, kitchen sponges, and colanders, for example.



Rule number three: Whenever possible make sure that meat and egg-based foods are cooked through. Of course, that doesn’t mean you have to

interrupt your romantic dinner to stick the tiramisu in the microwave. If you are planning a dish of that sort, make sure you always use good-quality, fresh eggs and always store them at a temperature of less than 50 degrees Fahrenheit (10 degrees Celsius).

Rule number four: Think beyond the kitchen. Anyone who has had to rush to the toilet after feeding their pet iguana and then themselves (without washing their hands properly) will remember my words: *Salmonella* bacteria are part of the normal gut flora of reptiles.

Helicobacter pylori—Humanity's First Pet

Thor Heyerdahl was a phlegmatic man with strongly held views. He observed ocean currents and winds. He was interested in ancient fishhooks and clothing made of tree bark. All this convinced him that the Polynesian islands were first colonized by seafarers from South America and Southeast Asia. He theorized that they could have used currents to help them reach the islands on rafts. At the time, no one thought it possible that a simple raft could survive a five-thousand-mile journey (eight thousand kilometers) across the Pacific. Heyerdahl was not a man to waste time trying to convince doubters with theoretical arguments. He went to South America, built a primitive raft out of balsawood logs, grabbed a couple of coconuts and cans of pineapple, and set out for Polynesia. After four months, he could safely say, "Yes, it is possible!"

Thirty years later, another scientist set off on an equally exciting expedition. But his journey did not take him across oceans; it took him to a small laboratory with neon strip lighting on the ceiling. There, Barry Marshall picked up a petri dish of liquid, placed it to his lips, and bravely swallowed its contents. His colleague observed him with interest as he did so. After a few days, Barry Marshall developed a stomach inflammation and could proudly say, "Yes, it is possible!"

Another thirty years went by before scientists in Berlin and Ireland made a connection between the research of these two very different pioneers. Marshall's stomach bug was destined to provide information about the first colonization of Polynesia. This time no one sailed an ocean and no one

drank a lab culture. Researchers asked a few desert-dwelling Aboriginals in Australia and highland tribesmen from New Guinea for a sample of their stomach contents.

It is a story about disproving prevailing paradigms, dedication to research, a tiny creature with a propeller, and a big, hungry cat.

The bacterium *Helicobacter pylori* lives in the stomachs of at least half of humankind. This insight is relatively new and was initially ridiculed. Why should an organism live in such an inhospitable environment? A cave full of acid and enzymes bent on breaking it down? It takes more than that to discourage *Helicobacter pylori*. This bacterium has developed two strategies that enable it to cope excellently with that harsh environment.

Firstly, the products of its metabolism are so alkaline that they can neutralize any acid in its immediate vicinity. Secondly, it burrows beneath the mucus membrane that protects the stomach from digesting itself with its acidic juices. This membrane usually has a gelatinous consistency, but *H. pylori* is able to liquefy it so that it can swim more easily through the mucoid lining. It has long threads of proteins it uses as flagella to whizz around.

Marshall and Warren believed *H. pylori* caused stomach inflammations (gastritis) and gastric ulcers. The prevailing scientific opinion at the time was that those stomach problems were psychosomatic in origin (as a result of stress, for example) or caused when the stomach secreted too much acid. Marshall and Warren had to both counter the preconception that nothing could survive in the acid environment of the stomach *and* prove that a tiny bacterium could cause diseases that were not traditional bacterial infections. Until that time, it was believed that bacteria could only infect wounds, and cause fevers and colds.

After the otherwise healthy Marshall deliberately swallowed *H. pylori* bacteria and gave himself gastritis, which cleared up after a course of antibiotics, it took another ten years before the scientific world accepted his discovery. Today, it is standard practice to test patients with stomach complaints for the presence of these bacteria. The patient is given a fluid to drink and if *H. pylori* bacteria are present in the stomach, they break down the ingredients of the fluid and a marked, odorless gas can be identified in the breath of the patient using a special machine. Drink, wait, breathe. A relatively simple test.

What the two scientists did not realize is that they had not only discovered a cause of illness, they had also discovered one of humankind's oldest pets. *H. pylori* bacteria have been living inside human beings for more than fifty thousand years, and they have evolved in tandem with us. When our ancestors began to migrate around the world, *H. pylori* went along for the ride and founded new populations, just like those human pioneers. Today, three African, two Asian, and one European type of this bacterium have been identified. The farther the population groups spread from each other in both space and time, the greater the difference between their stomach bacteria.

The slave trade transported the African types to America. In northern India, the Buddhist and Muslim populations have different strains in their stomachs. Families in industrialized nations often have their own family strain of *H. pylori*, while people living in societies with more contact between individuals, for example, in parts of Africa, have communal *H. pylori* strains.

One out of four North Americans is a carrier for *H. pylori.* Not everyone who carries it in their stomach is doomed to develop stomach problems, but most people who do have stomach problems have *H. pylori* to thank for their woes. This is because some *H. pylori* bacteria are more dangerous than others. Two factors are known to be responsible for the more virulent version. One is called CagA. CagA enables the bacteria to inject certain substances into our cells like a tiny syringe. The second factor is called VacA. VacA needles the cells of the stomach continuously, causing them damage that is eventually fatal to the cell. There is a much higher probability of developing stomach problems if the *H. pylori* microbes in the stomach possess the injecting-syringe or cell-damaging gene. If those genes are not present, *H. pylori* is much less harmful as it swims around in the stomach.

Although they share many similarities, each *H. pylori* bacterium is as unique as the person carrying it. These bacteria adapt to their host and change as she changes. Scientists can make use of this fact to trace who infected whom with the germ. Big cats have their own feline *Helicobacter*. Its name is *Helicobacter acinonychis*. The fact that it bears such a resemblance to human *Helicobacter* raises the question: who was eating

whom in prehistoric times? Was it a case of man eating tiger or tiger eating man?

Genetic analysis shows that the genes that were deactivated in the feline version of the bacterium were mainly those that would otherwise enable it to latch on to the cells of the human stomach—but the reverse was not the case. When devouring a prehistoric person, a large cat must also have devoured that person's stomach bacteria. These bacteria are not killed by even the sharpest of tiger teeth, so *Helicobacter* colonized the stomach of the predator and its descendants. A tiny bit of redress, at least.

But is *H. pylori* good or bad?

H. pylori Is Bad

By infiltrating our stomach's mucus membrane and swimming around in it, *H. pylori* weakens this protective barrier. As a result, the aggressive acids in our stomach digest not only our food, but a little bit of our own stomach, as well. If the bacteria also possess the injection-syringe or cell-damaging gene, our stomach cells have little hope. About one-fifth of people who harbor this bacterium develop tiny lesions in their stomach wall. Two-thirds of stomach ulcers and almost all ulcers in the small intestine are caused by an *H. pylori* infection. If the microbes can be wiped out with antibiotics, the patient's stomach problems disappear. A new product could soon provide an alternative to antibiotics: sulforaphane, which is contained in broccoli and similar vegetables. This substance is able to block the enzyme that *H. pylori* uses to neutralize gastric acid. Those who would like to try it as an alternative to antibiotics should make sure they use very high-quality broccoli and consult their doctor after two weeks to test whether their *H. pylori* population has really disappeared.

Constant irritation is never a good thing. We are all familiar with itchy insect bites. At some point we can no longer resist scratching them to make the itching stop, even though we know we will end up with a bleeding wound. Something similar happens with the cells of the stomach. A chronic inflammation means the cells are permanently irritated until they finally give up the ghost and break down. In older people, this can also be a cause of appetite loss.

The stomach has a battery of stem cells, which constantly replace lost cells. If these replacement manufacturers are overworked, they may begin

to make mistakes. Cancer cells are the result. Statistically, this does not look too serious: around 1 percent of *H. pylori* carriers develop stomach cancer. But if you bear in mind that half of humanity harbor these bacteria in their stomach, 1 percent turns out to be a pretty big number. The probability of developing stomach cancer without the presence of *H. pylori* is about forty times less than with it.

In 2005, Marshall and Warren received a Nobel Prize for their discovery of the connection between *Helicobacter pylori* and gastritis, stomach ulcers, and cancer. The journey from bacteria cocktail in Perth to celebratory cocktail in Stockholm took twenty years.

It took even longer for the connection between *Helicobacter pylori* and Parkinson's disease to be realized. Although doctors had known since the 1960s that patients with Parkinson's have an increased incidence of stomach problems, they did not know the nature of the connection between sore stomachs and trembling hands. It took a study of different population groups on the Pacific island of Guam to shed light on the subject.

In some parts of the island, there was an astonishingly high incidence of Parkinson's-like symptoms among the population. Those affected suffered from trembling hands, facial paralysis, and motor problems. Researchers realized that the symptoms were most common in areas where people's diets included cycad seeds. These seeds contain neurotoxins—substances that damage the nerves. *H. pylori* can produce an almost identical substance. When laboratory mice were fed with an extract of the bacteria, without being infected with the living bacterium itself, they displayed symptoms very similar to those of the cycad-eating Guamanians. Once again, not every *H. pylori* bacterium produces this substance, but for those people who harbor the ones that do, it is not good news.

In summary, it can be said that *H. pylori* can manipulate our protective barriers, irritate and destroy our cells, and manufacture toxins and damage our entire body by doing so. So, how has our vulnerable body been able to survive many millennia of infection with this bad bacterium? Why have these bacteria been so widely tolerated by our immune system for so long?

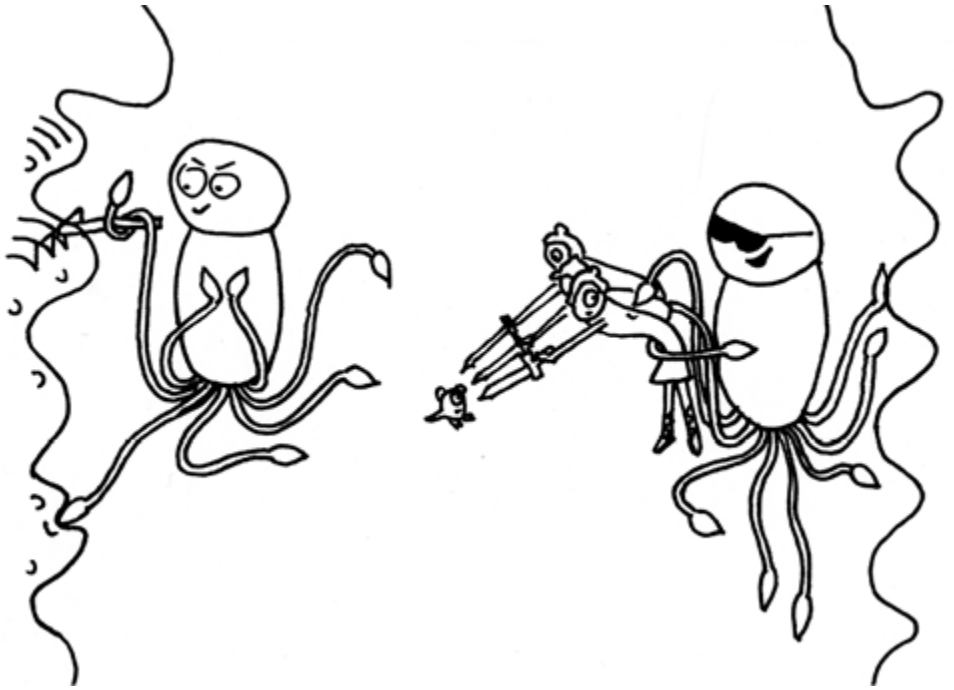
H. pylori Is Good

A large-scale study of *H. pylori* and its effects reached the following conclusion. The bacterium, especially that much-feared strain with the

injection-syringe gene, can also interact with the body in beneficial ways. After more than twelve years of observing over ten thousand subjects, it was concluded that carriers of this type of *H. pylori* do have an increased risk of stomach cancer, but their risk of dying of lung cancer or a stroke was much lower. In fact, it was only half that of other subjects in the study.

Even before this study, scientists had already suspected that a bacterium that has been tolerated for so long cannot be only bad. They had shown in experiments with mice that the *H. pylori* bacterium provides a reliable protection against childhood asthma. When the mice were given antibiotics, this protection disappeared and the infant rodents stood a chance of developing asthma again. When the bacterium was given to adult mice, the protective effect was still present but much less pronounced. You might say mice are not people, but this observation fits very well with the general trend noticed in industrialized countries in particular. Rates of asthma, allergies, diabetes, and neurodermatitis have risen as rates of *H. pylori* have fallen. This observation is far from constituting proof that *H. pylori* is the sole protection against asthma, but it may be part of the overall picture.

The theory suggested to explain this correlation is that this bacterium teaches our immune system to stay cool. *H. pylori* latches onto our stomach cells and by doing so causes large numbers of regulatory T-cells to be produced. Regulatory T-cells are immune cells whose job is to place a calming hand on the shoulder of the immune system when it flies off the handle like a drunk in a crowded nightclub. The T-cells say to the immune system, “Let us deal with this, mate.” As the name implies, these cells regulate the immune system’s reactions.



While the irate immune system is still shouting, “Get out of my lungs you bloody pollen-thing!” and showing its readiness to fight by giving us swollen, red eyes and a runny nose, the regulatory T-cells say, “Oh come on, immune system, that was a bit of an overreaction. The pollen-thing is only looking for a flower to pollinate. It’s just landed here by mistake. That’s more of a problem for the pollen grain than for us. It will never find its flower now.” The more of these sensible cells there are at work, the more chill the immune system will be.

When *H. pylori* causes a particularly large number of these cells to be produced by one mouse, another mouse’s asthma can be improved simply by transplanting those cells to it. That must be an easier solution than training a mouse to use a tiny little inhaler!

The incidence of eczema seems to be reduced by about one-third in people who harbor *H. pylori*. Increases in inflammatory gut disease, autoimmune problems, and chronic inflammations may also be a modern trend caused by the fact that we often unwittingly wipe out something that has protected us for millennia.

H. pylori Is Good and Bad

H. pylori are bacteria with many capabilities. They can't be labeled simply good or bad. It always depends on what exactly the bacterium does inside us. Is it manufacturing dangerous toxins, or is it interacting with our body to protect it in some way? Are our cells constantly irritated, or can we produce enough gastric mucus for both its needs and our own? What part is played by agents that irritate the stomach's mucus membrane, such as painkillers, cigarette smoke, alcohol, coffee, and stress? Is it a combination of all these that is responsible for stomach ulcers—because our little pets don't like them?

The World Health Organization recommends people with stomach problems should get rid of the potential culprits. If stomach cancer, certain lymphomas, or Parkinson's disease run in the family, it is also a good idea to offload *H. pylori*.

Thor Heyerdahl died in Italy in 2003 at the age of eighty-eight. Had he lived just a couple of years longer, he would have seen his theory about the colonization of Polynesia confirmed by studies of *H. pylori* strains. Asian strains of *H. pylori* conquered the New World in two waves, via the Southeast Asian route. But his theory about South American origins has not yet been proven. Who knows what bacteria still remain to be discovered before Heyerdahl's theory is confirmed by a micro-biological voyage of discovery?

Toxoplasmata—Fearless Cat Riders

A thirty-two-year-old woman cuts her wrists with a razor blade from the discount drugstore. It's the thrill that makes her do it.

A fifteen-year-old racing-car fan crashes into a tree at full tilt. And dies.

A rat drapes itself over the cat's food dish in the kitchen, presenting itself as a delicious meal.

What do these three have in common?

They are all failing to heed the internal signals that aim to preserve the huge community of cells that makes up living creatures. This community only wants the best for us. These three individuals seem to be pursuing

interests at odds with those of their body—interests that may well have come out of a cat's gut.

Cat's guts are the home of *Toxoplasma gondii*. These tiny little organisms consist of only one cell, but they are counted as animals. They carry much more complex genetic information than bacteria. Their cell walls are also constructed differently and they probably lead more exciting lives.

Toxoplasmata reproduce in the guts of cats. The cat acts as their definitive host and all the other animals that toxoplasmata use temporarily as taxis to take them from cat to cat are defined as intermediate hosts. A cat can get toxoplasmata only once in its life, and the cat is a danger to people only during that time of infection. Most older cats already have their toxoplasmata infection behind them and so cannot harm us anymore. During a fresh infection, toxoplasmata are found in the animal's feces. They mature in the cat litter for about two days before they are ready to infect their next host. If no cat happens to pass by but a dutiful, cat-owning mammal comes and cleans the litter, these tiny protozoa seize the opportunity. The microscopic creatures in the cat's feces can wait up to five years to infect another definitive host. Their intermediate host does not necessarily have to be a human cat-lover. Cats and other animals roam through gardens and vegetable patches and sometimes get killed. One of the main vectors of toxoplasma infection is raw food. The probability, in percent, of your having toxoplasmata yourself is about as high as your age in years. On a global scale, about one-third of humans harbor them.

Toxoplasma gondii are counted as parasites because they cannot live on just any little patch of earth and absorb water and plant tissue—they need a little patch of organism to live on. As humans, we call such creatures parasites because we get nothing in return. At least, nothing positive, like monthly rent or affection. Quite the opposite, in fact—some can harm us by means of a kind of human pollution.

They do not have any overly negative effects on healthy adult hosts. Some people have mild, flu-like symptoms, but most notice nothing. After the acute infection phase, the toxoplasmata move into tiny apartments in our tissue and enter a kind of hibernation state. They will never leave us for the rest of our lives, but they are quiet little lodgers. Once we have been through this, we can never be reinfected. We are already occupied, so to speak.

However, an infection like this can have drastic consequences for pregnant women. The parasites can reach an unborn child via the mother's bloodstream. The immune system is not yet familiar with them and is not fast enough to catch them. This does not necessarily always happen, but when it does, it can cause serious damage and even a miscarriage. If the infection is detected early enough, it can be treated with medication. But the chances of that are slim, since most people do not notice when they become infected. And in many countries, for example, a toxoplasma scan is not part of the standard set of pregnancy examinations. If your gynecologist starts asking strange questions like "Do you own a cat?" at your initial pregnancy examination, don't brush the question off as meaningless small talk—she's clearly an expert in her field.

Toxoplasmata are the reason your cat's litter should be changed every day if there is a pregnant woman in the house (but not by her!), why raw food should be avoided by mothers-to-be, and why fruit and vegetables should always be washed. Toxoplasmata cannot be transferred from person to person. Infection can only come from the little residents of a freshly infected cat's gut. But, as mentioned earlier, they can survive for a long time, even on the hands of cat owners. Once again, good old hand washing is the best defense.

So far, so good. All in all, toxoplasmata seem to be unpleasant but otherwise unimportant little critters if you don't happen to be pregnant. And, for many years, no one paid them much attention—but Joanne Webster's fearless rats changed all that. In the 1990s, Joanne Webster was a researcher at Oxford University. She devised a simple but ingenious experiment. She placed four boxes in a small enclosure. In one corner of each of these boxes, she placed a small bowl containing a different liquid: rat urine, water, rabbit urine, and cat urine. Even rats that have never seen a cat in their lives avoid cat urine. They are biologically programmed to think, "If someone peed there who might want to eat you, don't go there." Furthermore, rodents have a general motto that goes something like this: "If someone places you in an enclosure with boxes containing urine, be on your guard." Under normal circumstances, all rats behave the same way. They briefly explore the unfamiliar environment and then withdraw into one of the boxes with the less threatening urine in it.

But Webster found there were exceptions. There were rats that suddenly displayed completely atypical behavior. They inquisitively explored the whole enclosure, apparently oblivious to risk, even defying their instincts and entering the box containing the bowl of cat urine and hanging out there for a while. After observing them for longer, Webster was even able to conclude that they seemed to prefer the cat-urine box to the others. Nothing seemed to interest them more than cat pee.

A smell that should have registered in their brain as sign of mortal danger was suddenly perceived as attractive and interesting. These animals had become uninhibited seekers of their own downfall. Webster knew that there was only one difference between these rats and normal specimens—they were infected with toxoplasmata. This is an incredibly clever move on the part of the tiny parasites. They cause the rats offer themselves as food to their definitive hosts!

This experiment caused such consternation in the scientific community that it was repeated in other laboratories around the world. Scientists wanted to make sure the results were not a fluke so they tested to see whether their own lab rats would act in the same way if they were infected with toxoplasmata. And they did. The experiment is now considered flawless and scientifically sound. Scientists also discovered that the change in behavior was related only to the rats' response to cat urine, while dog urine elicited the expected avoidance behavior.

These results whipped up a storm of debate. How could such tiny parasites influence the behavior of little mammals so drastically? To die or not to die? That is a huge question that any organism worth its salt should be able to answer—as long as there is no parasite on the decision-making committee. Surely?

It was not much of a leap from the little mammal to a larger mammal (that is to say, to human beings). Might it be possible to find human candidates who succumb to a kind of "feed myself to the cat" instinct in the form of inappropriate reflexes, reactions, and fearlessness? One approach to finding an answer to this question was to test the blood of people who had been involved in traffic accidents. The quest was to find out whether more of the unfortunate road users would turn out to be toxoplasma carriers than members of society who had not been involved in an accident.

The answer was yes. The risk of being involved in a traffic accident is higher among toxoplasma carriers, especially when the infection is in the active early stage rather than the later dormant stage. Three small initial studies were followed by a large-scale investigation, and all of them confirmed these results. The large-scale study involved taking blood samples from 3,890 Czech army recruits and testing them for toxoplasmata. The recruits were monitored in the following years and the number of accidents they were involved in was recorded and analyzed. Severe toxoplasma infection in conjunction with a particular blood group (rhesus negative) turned out to be the highest risk factor. Blood groups can indeed play an important role in parasite infections—some groups offer greater protection than others.

BUT HOW DOES our lady with the razor blade fit in to all this? Why is she not horrified by the sight of her own blood? Why is the feeling of slicing through her skin, flesh, and nerves processed not as painful but rather, as thrilling? How can pain have become the hot sauce in the otherwise bland soup of her everyday life?

There are various ways of approaching this question. One of them is to look at toxoplasmata. When we are infected with them, our immune system activates an enzyme (IDO) to protect us from these parasites. IDO breaks down a substance that the invaders like to eat, forcing them to enter the less active, dormant state. Unfortunately, this substance is also one of the ingredients needed to produce serotonin. (Remember: a lack of serotonin is associated with depression and anxiety disorders.)

If the brain lacks serotonin because IDO has snatched it all away from under the parasite’s nose, our mood can be affected negatively. In addition, nibbled-on precursors of serotonin can dock onto certain receptors in the brain and cause symptoms like lethargy. These are the same receptors as those targeted by painkillers—the result is indifference and sedation. It can take quite drastic measures to drag the brain out of that state of torpor so it can feel emotions keenly again.

Our body is a clever body. It carries out a risk–benefit analysis. When a parasite needs to be combated in the brain, the brain’s owner is likely to be in a bad mood. Activating IDO is usually a kind of compromise. The body occasionally uses this enzyme to snatch food away from its own cells. IDO is

more highly activated during pregnancy, but only near the interface between mother and child. There, it snatches the food away from immune cells. That weakens them, making them react more mildly to the semi-alien presence of the baby.

Would the lethargy triggered by IDO be enough to drive someone to suicide? To put the question another way, what does it take to make people think about killing themselves? Where would a parasite need to start if it wanted to switch off our natural fear of harming ourselves?

Fear is associated with a part of the brain called the amygdala. Certain fibers run directly from the eyes to the amygdala, so the mere sight of a spider can trigger an immediate reaction of fear. This connection exists even in blind people whose visual cortex has been damaged by an injury to the back of the head. They no longer see the spider, but they still feel it emotionally. So, our amygdala plays a major role in the development of fear. If the amygdala gets damaged, a person can become fearless.

Examinations of intermediate toxoplasmata hosts show that the apartments the toxoplasmata occupy to hibernate in are mainly found in the muscles and the brain. Those in the brain are found in three locations. In descending order of frequency, these are the amygdala, the olfactory center, and the area of the brain directly behind the forehead. As we know, the amygdala is responsible for the perception of fear. The olfactory center could be responsible for the rat's new-found love of cat urine. The third area is slightly more complex.

This part of the brain creates possibilities by the second. If a research subject is wired up to a brain scanner and confronted with questions about faith, personality, or morality, or if he is asked to complete complex and challenging cognitive tasks, lively activity is recorded in this region. One theory proposed by brain researchers is that this indicates that this area of the brain is drawing up many designs every second. "I could believe in the religion followed by my parents. I could start licking the desk in front of me during this conference. I could read a book and have a cup of tea. I could dress the dog up in a funny costume. I could film myself singing a jolly song. I could drive my car at breakneck speed. I could reach for that razor blade..." There are hundreds of possibilities every second, but which will win through and which will be carried out?

So, if you are a parasite with a plan, it makes sense to settle here. From here, it might be possible to promote self-destructive tendencies and weaken the mechanisms that suppress these courses of action.

Researchers wouldn't be researchers if they hadn't come up with the idea of repeating Joanne Webster's experiment with human beings. So they had humans sniff different animals' urine. Men and women who were toxoplasma carriers had a different reaction to the smell of cat pee from those who were parasite-free. Men liked the smell considerably more, women less.

Smell is one of our most basic senses. Unlike taste, hearing, or vision, smells are not checked out before they make their way to our consciousness. Strangely, we can dream all sensory experiences except smells. Our dreams are always odorless. Truffle pigs know just as well as toxoplasmata that smells can trigger an emotional response. As it happens, the scent of a truffle is pretty similar to the scent of a sexy truffle pig male. When an infatuated female truffle pig smells a sexy male truffle pig hiding under the earth, she will dig and dig until... she discovers a disappointingly unsexy fungus for her owner. I think the astronomical price of truffles is more than justified when you consider how frustrating such a find must be for a poor sow. Anyway, the point is that smells can stimulate attraction.

Some shops exploit this phenomenon. Economists call it scent marketing. One American clothing manufacturer even uses sex pheromones to attract potential customers. In Frankfurt, where I live, you can often see long lines of teenagers outside the store's darkened and pheromone-scented entrance. If the shopping precinct were closer to areas with free-ranging pigs, some pretty entertaining scenes might result.

SO, IF ANOTHER organism can make us perceive smells differently, couldn't it also influence other sensory impressions?

There is a well-known illness whose main symptom is false sensory perceptions: schizophrenia. For example, people suffering from schizophrenia might feel like an army of ants is crawling all over their back, although there are no such insects anywhere nearby. They hear voices and obey their commands, and they can be extremely lethargic. About half to one percent of people suffer from schizophrenia.

There is much about the clinical picture of schizophrenia that is still unclear. Most drugs used to treat it do so by deactivating a signal transmitter in the brain that is overabundant in people with schizophrenia: dopamine. Toxoplasmata possess genes that influence the production of dopamine in the brain. Not all people who suffer from schizophrenia are parasite carriers—so that can be ruled out as the sole cause—but the proportion of carriers among those who suffer from schizophrenia is about twice that among those who do not.

Toxoplasma gondii could, therefore, influence us via the fear, smell, and behavioral centers of the brain. A higher risk of being involved in an accident, attempting suicide, or suffering from schizophrenia indicates that an infection affects at least some of us. It will take some time before discoveries like these have consequences for standard medical practice. Suspicions need to be scientifically proven and further research into possible treatments is needed. This insistence of science on time-consuming validation processes can cost lives. Antibiotics, for example, did not appear in our pharmacies until decades after they were discovered. But this caution can also save lives. Thalidomide and asbestos could easily have been tested for a little bit longer before entering the market.

Toxoplasmata can influence us far more than we would ever have thought possible just a few years ago. And they have rung in a new scientific age. An age in which a crude lump of cat feces can show us how susceptible our lives are to change. An era in which we are just beginning to understand just how complex the connections are between us, our food, our pets, and the microscopic world in, on, and around us.

Is this spooky? Well, maybe a little bit. But isn’t it also exciting to see how we are gradually decoding processes that we used to believe were part of our inescapable destiny? This could help us to grab the risks by the horns and defy them. Sometimes, it takes nothing more than a scoop of cat litter, a well-cooked chicken, and properly washed fruit and veggies.

Pinworms

There are some little white worms that like to live in our gut. Over many centuries, they have adapted their behavior to live with us. Half the world's population has had a visit from these worms at some time or other. Some people never even notice. For others, it's an embarrassing infestation they'd rather not talk about. If you look at just the right moment, you can even see them giving us a wave out of the anus. They are 0.2 to 0.4 inches (5 to 10 millimeters) long, and white, and they sometimes have a pointed end. They look a little like the vapor trails left by jets in the sky except they don't get longer and longer. Anyone who has a mouth and a finger can get these parasites, which are also known as threadworms. Finally, there's an advantage to being fingerless and/or mouthless!

Let's put the cart before the horse, or rather, the worm. A lady-worm looking for a place to lay her eggs wants to make sure they will have a secure future. And such a place is not so easy to reach. A pinworm egg has to be swallowed by a human being, then hatch in the small intestine so that it can reach the large intestine by the time it is a grown-up worm. But our mother-worm-to-be lives in the lower reaches of the digestive tract with everything moving in the wrong direction for her needs. So she wonders how she is ever going to get back to her host's mouth to give her eggs the start in life that they need. Here she makes use of the only kind of intelligence such a creature has at her disposal—the intelligence of adaptation. Whether this is the origin of the word "brown noser" or not is open to question.

Female pinworms know when we are still, lying down, and too comfortable to rouse. That's exactly when they set off toward the anus. They lay their eggs in the many little creases around the anus and wriggle around until it starts to itch. They then slip quickly back inside the gut, because experience has taught them that soon a hand will appear and finish off the job. Under the bedclothes, the hand heads for the backside, targeting that itch. The same neural pathways that passed on the itch now give the instruction to scratch. We obey the instruction, thereby providing the pinworm's children with an express connection to the mouth area.

When are we least likely to go and wash our hands after scratching our behind? When we are oblivious to all this action because we are asleep or too sleepy to get up and head for the bathroom. And that is pinworm egg-laying time. It's clear what that next dream about sticking your finger in a

yummy chocolate cake will mean. It will mean that those eggs are heading to their ancestral home: your mouth. That might sound gross, but it's not so very different from eating chickens' eggs. Only chickens' eggs are bigger and usually cooked.

Organisms that move into our gut uninvited and implement their plans for progeny there get a bad rap from us. And we often avoid talking about them with others. It's as if we feel we have been a bad manager for our body, failing to lay down the law properly and letting any old strangers take up residence without interviewing them first. But pinworms are not just any old strangers. They are guests who wake the manager in time for morning exercises and then give their host a massage to stimulate the immune system. Furthermore, they steal very little of our food.

It is not good to keep these parasites as permanent guests, but once in a lifetime is fine. Scientists suspect that when kids have had worms, they are less likely to contract severe asthma and diabetes in later life. So welcome, Mr. and Mrs. Pinworm, come on in! But don't outstay your welcome, please. An uncontrolled attack of worms can have three rather unwelcome consequences.

1. Lack of a good night's sleep can lead to concentration problems, nervousness, or irritability during the day.
2. What the worms don't want is to lose their way—and we don't want them to either. When worms get into places they don't belong, they have to go. Who wants a pinworm with a bad sense of direction, after all?
3. Sensitive guts, or those containing overactive worms, can become irritated. Worms have a tendency to cause irritation anyway. There are many problems this can cause: not going to the toilet often enough, going to the toilet too often, abdominal cramps, headaches, nausea, or none of the above.

If a worm host has any of these symptoms, a visit to the doctor is essential! The doctor will ask you to put sticky tape to a use you never learned in arts and crafts lessons in elementary school. Some doctors are more charming about it than others, but, in essence, what they will tell you to do is to spread your cheeks, stick tape to your anus and the surrounding area, pull it off again, bring it to the surgery, and hand it over to the receptionist.

Worm eggs are small and round and adhere well to sticky tape. Searching for eggs on Easter Sunday morning would be a lot more efficient if you had a great big egg-magnet that attracted all the eggs from the garden. Since worm eggs are so much smaller than Easter eggs, it makes sense to use a trick like this. The sticky-tape egg hunt has to take place in the morning, as that's when most eggs are there. And it is not a good idea to flush out or sweep clean the worm garden before you hunt for the eggs. So the first thing that comes into contact with the region in the morning should be those strips of sticky tape.

The doctor will examine the fruits of your labors under the microscope, hunting for little oval eggs. If they are already developing into larvae, they will have a line down the middle. The doctor can then prescribe the right medication and your pharmacist will help you win the battle to get rid of your unwanted guests. The typical medication prescribed—let's call it mebendazole for the sake of argument—works on the tit-for-tat principle we all know from kindergarten: if you bother my gut, I'll bother yours.

The medication makes its way from mouth to rectum and meets our renegade squatters along the way. Mebendazole is much more harmful to a worm's gut than it is to ours. It places the worms on a forced diet, denying them all access to sugar. Sugar is the stuff of life for worms, so this will be the last diet they ever go on. It's a bit like trying to get rid of unwanted guests by not offering them anything more to eat.

Pinworm eggs live for a long time. If you have worms and can't keep your hands away from your mouth, you should at least try to reduce the number of eggs in the area to a minimum. Bedclothes and underwear should be changed every day and washed at 140 degrees Fahrenheit (60 degrees Celsius) or hotter, regular hand washing is essential, and intense itching might be better treated with creams than by scratching. My mother is convinced that worms can be eliminated by swallowing a whole clove of garlic once a day. I have not been able to find any scientific studies to prove this, but nor are there any studies about what temperature necessitates the wearing of warm jackets and my mother is always right about that! If all this fails, do not despair. Go back to your doctor and be proud of having such an inviting gut.

Of Cleanliness and Good Bacteria

WE ALWAYS WANT to protect ourselves from harm. Few people would choose to have *Salmonellae* or a nasty *H. pylori*. Even though we have not yet identified them all, we know already that we'd rather not have chubby bacteria or microbes that cause diabetes or depression. Our greatest protection against them is cleanliness. We are careful about eating raw food, kissing strangers, and washing our hands to rid them of anything that might spread disease. But cleanliness is not always what we imagine it to be.

Cleanliness in our gut is something akin to cleanliness in a forest. Even the most conscientious of cleaners would not dream of taking a mop to the forest floor. A wood is clean if the beneficial plants it contains are in healthy equilibrium. We can help the forest along by sowing seeds and hoping new plants will take root. We can identify favorite or useful plants in the forest and nurture them to help them grow and multiply. Sometimes, there are nasty pests. Then, careful consideration is in order. If the situation is desperate, chemicals might be the answer. As their name implies, pesticides are great at killing pests, but it is not a great idea to spray them round like air freshener.

Clever cleanliness begins with our everyday routines—but what is well-advised caution and what is excessive hygiene? There are three main tools for keeping our insides clean. Antibiotics can rid us of acute pathogens, while prebiotic and probiotic products can promote beneficial elements. *Pro bios* means "for life." Probiotics are edible living bacteria that can make us healthier. *Pre bios* means "before life." Prebiotics are foodstuffs that pass undigested into the large intestine, where they feed our beneficial bacteria so that they thrive better than bad bacteria. *Anti bios* means "against life." Antibiotics kill bacteria and are our saviors when we have picked up a pack of bad bacteria.

Everyday Cleanliness

The fascinating thing about cleanliness is that it is mostly in the head. A peppermint tastes fresh, clean windows look clear, and we love slipping into a freshly made bed after a hot shower. We like the smell of clean things. We like to run our hands over smooth, polished surfaces. We find comfort in the idea that we are protected from an invisible world of germs if we use enough disinfectant.

In Europe 130 years ago, it was discovered that tuberculosis is caused by bacteria. This was the first time the public took notice of bacteria—and they were seen as bad, dangerous, and, most worryingly, invisible. It was not long before new regulations were introduced in European countries: patients were isolated so they could not spread their germs; spitting was forbidden in schools; close physical contact was discouraged; and warnings were issued against "the communism of the towel!" People were even advised to limit kissing to "the erotically unavoidable." That might sound funny to us today, but those ideas put down deep roots that can still be felt in our modern Western society: spitting is still frowned upon, we are still reluctant to share towels and toothbrushes, and we keep a greater physical distance in our dealings with others than most cultures.

Preventing deadly disease by banning pupils from spitting at school seemed like a simple and effective idea. We internalized it in our culture as a social rule. Those who did not comply were despised as a danger to everyone's health. This attitude was passed on from parent to child, and public spitting became a social taboo. Cleanliness really was thought to be next (in importance) to godliness; people craved a sense of order in a life full of chaos. The anthropologist Mary Douglas summed this up in her book *Purity and Danger* with the phrase, "Dirt is matter out of place."

Bathing as a way of keeping the body clean was a privilege of the rich even up to the beginning of the twentieth century. It was around that time that dermatologists in Germany began to call for "a bath a week for every German!" Large companies built bathhouses for their employees and encouraged personal hygiene by issuing them with free towels and soap. The tradition of the weekly bath did not really take hold until the 1950s. Then, typical families took their bath on a Saturday evening, one after another in the same bathwater, and hard-working Dad often got to go in the tub first. Originally, personal cleanliness meant ridding the body of unpleasant smells and visible dirt. As time went on, this concept became

increasingly abstract. It's hard for us today to imagine this once-a-week family bathing routine. We spend money on disinfectants to get rid of things we can't even see. The surface in question looks exactly the same after cleaning as it did before—yet just knowing it is clean is extremely important to us.

The news media tell us horror stories about dangerous flu viruses, multi-drug-resistant superbugs, and EHEC-contaminated food. When food contamination scares such as tainted salad recalls are in the news, some people react by giving up lettuce while others type "full body decontamination shower" into Google. Different people deal with fear in different ways. Dismissing this as hysteria is too easy. It makes more sense to try and understand where these fears come from.

Fear-driven hygiene involves attempting to clean everything away or kill it off. We don't know what it might be, but we assume the worst. When we clean obsessively, we do indeed get rid of everything—both bad and good. This cannot be a good kind of cleanliness. The higher the hygiene standards in a country, the higher that nation's incidence of allergies and autoimmune diseases. The more sterile a household is, the more its members will suffer from allergies and autoimmune diseases. Thirty years ago, about one person in ten had an allergy. Today that figure is one in three. At the same time, the number of infections has not fallen significantly. This is not smart hygiene. Research into Nature's huge range of bacteria has led to a new understanding of what cleanliness should mean. It is no longer defined as the attempt to kill off potential dangers.

More than 95 percent of the world's bacteria are harmless to humans. Many are extremely beneficial. Disinfectants have no place in a normal household. They are appropriate only if a family member is sick or the dog poops on the carpet. If a sick dog poops on the carpet, there are no holds barred—bring on the steam cleaners, disinfectant by the bucket-load, or a small flame thrower, perhaps. That might even be fun! But if the floor is just covered in dirty footprints, water and a drop of cleaning fluid are all you need. That combination is already enough to reduce the bacteria population of your floor by 90 percent, and it leaves the normal, healthy population of the floor a chance to recolonize the territory. What remains of any harmful elements is so little as to be negligible.

The aim of cleaning, then, should be to reduce bacteria numbers—but not to zero. Even harmful bacteria can be good for us when the immune system uses them for training. A couple of thousand *Salmonella* bacteria in the kitchen sink are a chance for our immune system to do a little sightseeing. They become dangerous only when they turn up in greater numbers. Bacteria get out of hand when they encounter the perfect conditions: a protected location that is warm and moist with a supply of delicious food. There are four recommended strategies for keeping them in check: dilution, temperature change, drying, and cleaning.

Dilution

Dilution is a technique we also use in the laboratory. We dilute bacteria with fluids and administer drops with different concentrations of bacteria to wax moth larvae, for example. Wax moth larvae change color when they get sick. That makes them a good indicator of the concentration of bacteria required to cause illness. For some, it's a little as a thousand per drop of fluid, for others, as many as ten million.

One example of bacteria dilution in the home is washing fruit and vegetables. Washing dilutes most soil-dwelling bacteria to such a low concentration that they become harmless to humans. Koreans add a little vinegar to the water to make it slightly acidic and just that bit more uncomfortable for any bacteria. Airing a room is also a dilution technique.

If you dilute the bacteria on your plates, cutlery, and cutting board nicely with water, then wipe them over with a kitchen sponge before putting them away, you may as well have licked them clean with your tongue. Kitchen sponges offer the perfect home for any passing microbe—nice and warm, moist, and full of food. Anyone looking at a kitchen sponge under the microscope for the first time usually wants to curl up on the floor in a fetal position, rocking back and forth in disgust.

Kitchen sponges should only be used for cleaning the worst of the dirt off. Plates, cutlery, and so on should then be rinsed briefly under running water. The same is true for dish towels or drying-up cloths if they never get a chance to dry out. They are more useful for spreading a nice even layer of bacteria on your utensils than for drying them. Sponges and cloths should be thoroughly wrung out and allowed to dry—otherwise they become the perfect place for moisture-loving microbes.

Drying

Bacteria cannot breed on dry surfaces. Some cannot survive there at all. A freshly mopped floor is at its cleanest after it has dried. Armpits that are kept dry by antiperspirants are less cozy homes for bacteria—and fewer bacteria produce less body odor. Drying is a great thing. If we dry food it keeps for longer before it rots. We use this to our advantage: just think of foodstuffs like pasta, muesli, crisp bread, dried fruit (such as raisins), beans, lentils, and dried meats.

Temperature

In many parts of the world, the environment is refrigerated naturally once a year. From a bacteriological point of view, winter is the real spring clean! Refrigerating food is an extremely important part of our daily lives, but a fridge contains so much food that it remains a paradise for bacteria even at low temperatures. The optimum temperature for your fridge is something below 41 degrees Fahrenheit (5 degrees Celsius).

Let’s move on to another household appliance—the washing machine. Most washing machine programs use the dilution principle to clean our clothes and that is sufficient. However, damp kitchen cloths, a load of underpants, or sick people’s laundry should be washed at 140 degrees Fahrenheit (60 degrees Celsius) or more. Most *E. coli* bacteria are killed by temperatures above 104 degrees Fahrenheit (40 degrees Celsius), and 158 degrees Fahrenheit (70 degrees Celsius) is enough to kill off tougher *Salmonella* bacteria.

Cleaning

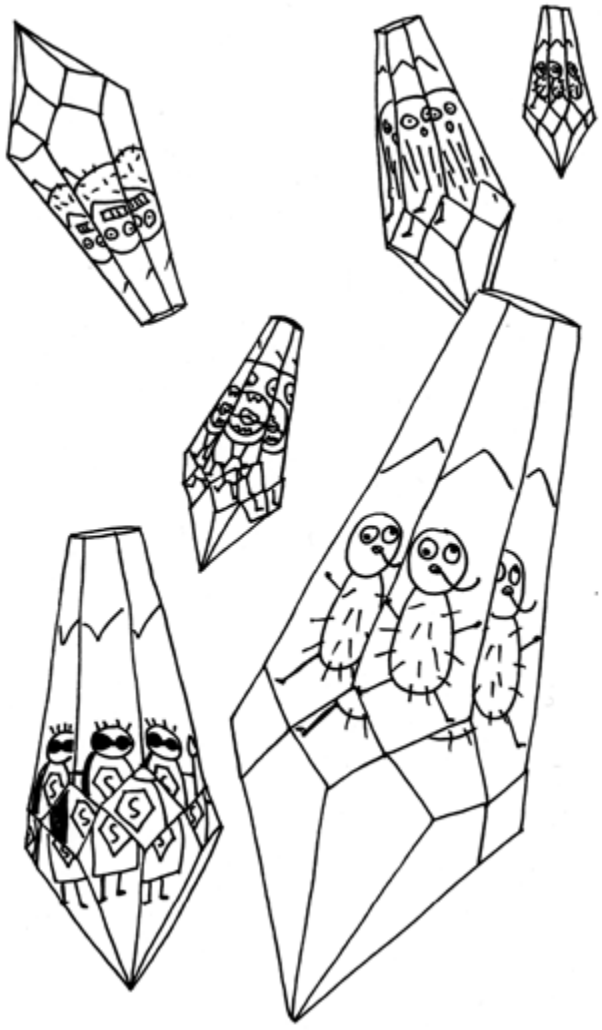
Cleaning means removing a film of fats and proteins from surfaces. Any bacteria living in it or under it will be removed along with the film. We usually use water and cleaning fluid to achieve this. Cleaning is the technique of choice for all living spaces, kitchens, and bathrooms.

This technique can be taken to the absolute extreme. That is sensible when you are manufacturing medical drugs that are destined to be pumped straight into a patient’s veins (such as infusions). The drugs need to be absolutely free of all bacteria. This is achieved in pharmacological laboratories by using iodine, for example. Iodine sublimates, which means

it transitions from a solid, crystalline state to a gaseous vapor in the presence of heat without passing through a liquid phase. So pharmacologists heat up iodine until the entire production lab is veiled in a blue vapor.

It sounds like the simple principle of the steam cleaner, but there is more to it than that. Iodine can also desublimate. To make this happen, the room is cooled and the vapor immediately recrystallizes. Millions of tiny crystals form on all surfaces and even in mid-air, trapping every microbe as they do so, locking them up in a crystal prison as they fall to the ground. Workers pass through several airlocks and disinfection chambers, dress up in germ-free bodysuits, and sweep up the iodine crystals.

In principle, we use the same system when we use hand cream. We trap microbes in a film of fat and hold them captive there. When we wash the film off, we rinse the bacteria away with it. Since our skin produces a natural coating of fat, soap and water are often enough to achieve this effect. Some of the fat layer remains, aiding its replenishment after washing. Too frequent hand washing makes no sense—and the same is true of too frequent showering. If the protective fat layer is rinsed away too often, our unprotected skin is exposed to the environment. That gives odor-producing bacteria a better foothold, making us smell more pungently than before, creating a vicious circle.



Bacteria trapped in iodine crystals.

New Methods

A team from Ghent in Belgium is currently trying out a brand-new method. The researchers are attempting to use bacteria to combat body odor. They disinfect volunteers' armpits, spread them with odorless bacteria, and start the stopwatch. After a couple of minutes, the subjects are allowed to put their shirts back on and go home. The volunteers return repeatedly to the laboratory, where experts sniff their armpits. The initial results are quite promising—the odorless bacteria manage to banish their smelly colleagues in many of the subjects' armpits.

Not far away, across the border in Germany, the same method is in use in the public toilets of the small town of Düren. A company is using a mixture

of bacteria to clean the toilets. The odorless bacteria occupy the places normally colonized by the bugs that create that all-too-familiar public toilet smell. The idea of using bacteria to clean public conveniences is a brilliant one. Unfortunately, the company refuses to reveal the recipe for its cocktail of bacterial cleaners, so a scientific evaluation is impossible. However, the town of Düren seems to be faring very well with this experiment.

These new ideas about the use of bacteria illustrate one thing very clearly: cleaning does not mean annihilating all bacteria. Cleanliness is a healthy balance of sufficient good bacteria and a few bad ones. That means smart protection against real dangers and, sometimes, deliberate contamination with good bugs. With this in mind, we can perhaps better appreciate the wisdom of observations like that of the American writer Suellen Hoy, who says in her book *Chasing Dirt*, "From the perspective of a middle-class American woman (also a seasoned traveler) who has weighed the evidence, it is certainly better to be clean than dirty."

Antibiotics

Antibiotics are reliable killers of dangerous pathogens. And their families. And their friends. And their acquaintances. And distant acquaintances of their acquaintances. That makes them the best weapon against dangerous bacteria—and the most dangerous weapon against good bacteria. But who is it who manufactures most antibiotics? It's bacteria. Huh?

Antibiotics are the weapons used by both sides in the war between fungi and bacteria.

Ever since researchers discovered all this, pharmaceutical companies have been intensively farming bacteria. Huge tanks with a capacity of up to 26,500 US gallons (100,000 liters) are used to grow so many bacteria that their numbers can hardly be expressed in any meaningful figures. They produce antibiotics, which we purify and press into little tablets. The product sells well, especially in the United States. When researchers were planning a study of the effect of antibiotics on the flora of the gut, they were able to find only two people in the entire San Francisco Bay Area who had not taken antibiotics in the previous two years. In Germany, one person in

every four takes antibiotics once a year on average. The main reason for taking them is colds. This is like a knife in the heart of any microbiologist. Colds are often not even caused by bacteria, but by viruses! Antibiotics can work in three different ways: by peppering the bacteria with holes, by poisoning the bacteria, or by rendering the bacteria unable to reproduce. They have no effect on viruses at all.

So taking antibiotics to cure a cold is usually a complete waste of time. If they do bring about an improvement, this is due either to the placebo effect or to the work of the immune system in combating the cold virus. The senseless use of antibiotics does, however, kill many helpful bacteria, which can be harmful in itself. To avoid this, doctors can perform a procalcitonin test, which indicates whether cold-like symptoms are caused by a bacterial or viral infection. The test can be especially helpful to make sure children don't take antibiotics unnecessarily.

There is no reason not to take antibiotics when it is medically appropriate to do so. The benefits certainly outweigh the disadvantages, for example, in cases of severe pneumonia or for helping children get over a particularly bad infection with no long-term damage. In such cases, those little tablets can save lives. Antibiotics stop bacteria from reproducing, the immune system kills off any remaining pathogens, and we soon start to feel better. We have to pay a price for this, but in the final reckoning, it's a good deal.

The most common side effect is diarrhea. Even those who don't get diarrhea may notice that they leave a rather larger deposit in the morning toilet bowl than usual. To tell it like it is: a large portion of that pile is dead gut bacteria. The antibiotic tablet does not travel directly from mouth to blocked-up nose. It descends into the stomach and then on to the gut. Before it graduates from there into the bloodstream—and then to the nose, among other places—it peppers our microbe collection with holes, poisons our gut bacteria, and makes them sterile. The result is a formidable battlefield—you can see the casualties the next time you go to the toilet.

Antibiotics can alter our gut flora significantly. Our microbe collection becomes much less diverse and the abilities of the bacteria in it can change. Changes include the amount of cholesterol they can absorb, their ability to produce vitamins (like skin-friendly vitamin H), and the type of foodstuffs they can help us digest. Preliminary studies carried out at Harvard and in

New York have shown that the two antibiotics metronidazole and gentamicin cause particularly hefty changes in the flora of the gut.

Antibiotics can be problematic for children and old people. Their gut flora is already less stable and less able to recover after treatment with antibiotics. Research in Sweden showed that the gut bacteria of children were still significantly altered two months after taking antibiotics. Their guts contained more potentially harmful bacteria and fewer beneficial types like *Bifidobacteria* and *Lactobacilli.* The antibiotics used were ampicillin and gentamicin. The study involved only nine children, which means it is not particularly meaningful in scientific terms, but it remains the only study of its kind so far. So the results should be accepted with a degree of caution.

A more recent study of pensioners in Ireland revealed a clear dichotomy. Some gut landscapes recovered very well after a course of antibiotics, while others remained permanently altered. The reasons for this are still completely unclear. The ability to return quickly to a stable state following an extreme experience is described with same word by gut researchers and psychologists: resilience.

Even though antibiotics have been in use for more than fifty years, studies of the long-term effects can still be counted almost on one hand. The reason for this is technological: the equipment necessary for such

investigations has only been around for a couple of years. The only long-term effect that has been scientifically proven is drug resistance. For as long as two years after taking antibiotics, bad bacteria are still present in the gut, telling their great-great-great-... -grandchildren stories about the war.

These are the ones that resisted the antibiotics and survived. And with good reason. Bacteria develop resistance strategies. Some install tiny pumps in their cell walls to pump the antibiotic out like emergency workers pumping water out of a flooded cellar. Others prefer to disguise themselves so the antibiotics cannot recognize their surface and so cannot pepper them with holes. Yet others use their ability to split things—they build tools to cut the antibiotics to pieces.

The thing is that antibiotics rarely kill all bacteria. They kill certain communities depending on the toxins they use. There will always be some bacteria that survive and become experienced fighters. In the case of serious illness, these fighters can become a problem. The more resistances the bacteria have developed, the more difficult it is to get them under control again with antibiotics.

Every year, many thousands of people die because they are infected with bacteria that have developed resistances that no drug can counter. When their immune system is compromised—for example, after an operation—or if the resistant bacteria have got out of hand after a long course of treatment with antibiotics, the patient can be in real danger. Very few new drugs are in development, for the simple reason that it is not very profitable for pharmaceutical companies to do so.

SO HERE ARE four pieces of advice for anyone who wants to keep out of unnecessary antibiotic gut wars.

1. Do not take antibiotics unless it is really necessary. And if you do have to take them, then always complete the course. This is because resistance fighters who are less skilled will eventually give up the cause and succumb to the drug. So the only ones that remain are those that would never have been killed by the antibiotics anyway. But at least the rest will have been well and truly done in.
2. Choose organically farmed meat. Drug resistances differ from country to country. It is shocking to see how often these resistances correspond to the antibiotics used in large-scale animal farming. In countries like India

or Spain, for example, there is almost no regulation of the amount of antibiotics given to animals. This turns the animals' guts into giant breeding zoos for resistant bacteria. And people in such regions have significantly more infections with multi-drug-resistant strains. In other countries, regulations do exist, but even here the rules are ridiculously vague. This allows many vets to make a lot of money in the semi-legal antibiotics trade.

It was not until 2006 that the European Union banned the use of antibiotics in animal feed as performance enhancers. The kind of performance being enhanced here is the ability of an animal to not die of infections in a crowded and dirty pen. Antibiotics are a great way to "enhance" this "performance." In the United States, the Food and Drug Administration is working on a voluntary plan to phase out the use of some of these antibiotics in regular farming. In organic farming, the Department of Agriculture forbids the use of any antibiotics, and an animal given antibiotics—for example, to relieve suffering—must be removed from organic production.

If possible, it is worth spending that little extra—to prevent resistance-breeding zoos and for your peace of mind... and peace of gut. The dividends are not immediate, but it is an investment in a better future for us all.

3. Wash fruit and vegetables thoroughly. Animal feces are a popular fertilizer, and liquid manure is used in vegetable fields. In many countries, fruit and vegetables are not routinely tested for residues of antibiotics—and certainly not for multi-drug-resistant gut bacteria. Milk, eggs, and meat are usually tested to make sure they don't exceed certain limits. So err on the side of caution and wash your fruit and vegetables one extra time if you are not sure. Even tiny amounts of antibiotics can help bacteria develop resistances.
4. Take care abroad. One traveler in four returns home carrying highly resistant bacteria. Most disappear in a few months, but some lurk around for much longer. Special care should be taken in bacterial problem countries like India. In Asia and the Middle East, you should wash your hands regularly, and clean fruit and vegetables thoroughly—if necessary with boiled water. Southern Europe also has its problems. "Cook it, peel

it, or leave it" is not only a good rule for avoiding diarrhea, it also protects against unwanted resistant souvenirs for you and your family.

Are There Alternatives to Antibiotics?

Plants produce antibiotics that have functioned for centuries without causing resistances. (Fungi, such as the penicillin fungus, are not plants but opisthokonts, like animals.) When parts of plants snap off or become perforated, they need to produce antimicrobial substances at the location of the damage. If they did not do this, they would immediately become a feast for any bacteria in the vicinity. Pharmacies sell concentrated plant antibiotics to treat developing cold symptoms, urinary infections, and inflammations in the mouth and throat. Some products contain mustard seed or radish seed oil, for example, or chamomile and sage extract. Some can reduce the numbers of viruses as well as bacteria. That leaves our immune system with less to contend with, giving it a better chance of dealing with pathogens.

Such plant-based remedies are not the solution for serious illnesses or for illnesses that drag on with no noticeable improvement. In such cases, they can even be harmful because they encourage us to wait too long before turning to powerful antibiotics. In recent years, the incidence of heart and ear damage in children has increased. This is often due to the behavior of parents who want to protect their children from too much exposure to antibiotics. Such a decision can have damaging consequences. A well-informed doctor will not prescribe antibiotics for every little thing—but will tell you in no uncertain terms when they are really necessary.

Our relationship with antibiotics is an arms race: we use them to arm ourselves to the hilt when faced with dangerous bacteria, and they respond by arming themselves with even more dangerous resistances. Medical researchers should really be developing the next generation of weapons in this race. Every one of us accepts a trade-off when we take these drugs. We agree to sacrifice our good bacteria in the hope of getting rid of the bad. In the case of a minor cold, that's not a good deal; for serious illnesses, it's a trade that pays off.

There is no species protection program for gut bacteria. We can be pretty certain that we have annihilated many family heirlooms since the discovery of antibiotics. The places they leave vacant should be colonized by the best

candidates possible—probiotics, for example. They help the gut to return to a state of healthy equilibrium after danger has been averted.

Probiotics

We swallow many billions of living bacteria every day. They are on raw food, a few survive on cooked food, we nibble on our fingers without even thinking about it, we swallow our own mouth bacteria or kiss our way through the bacterial landscapes of others. A small proportion even survive the acid bath of the stomach and the aggressive digestive process to reach our large intestine alive.

No one knows the majority of these bacteria. They presumably do us no harm, or perhaps even benefit us in some way we have not yet discovered. A few are pathogens, but they usually cannot harm us because their numbers are just too small. Only a fraction of these bacteria have been thoroughly checked out by scientists and given the official seal of approval. These bacteria can proudly call themselves probiotics.

We often read the word “probiotic” on the yogurt we find on our supermarket shelves without having any real idea what it means or how they work. Most will recall television commercials telling us they strengthen our immune system, or showing us a constipated aunt relieved of her woes and recommending this brand to everyone she knows. That all sounds good. You don’t mind spending a little extra for a healthy product like that. And before you know it, those probiotics are in your shopping basket, then in your fridge, and eventually in your mouth.

People have been eating probiotic bacteria since time immemorial. Without them, we would not exist. A group of South Americans had to learn that through bitter experience. They had the clever idea of taking pregnant women to the South Pole to have their babies. The plan was that the babies born there could stake a claim to any oil future reserves as natives of the region. The babies did not survive. They died soon after birth or on the way back to South America. The South Pole is so cold and germ-free that the infants simply did not get the bacteria they needed to survive.

The normal temperatures and bacteria the babies encountered after leaving the Antarctic were enough to kill them.

Helpful bacteria are an important part of our life, and we are constantly surrounded and covered by them. Our ancestors had no idea of their existence, but they intuitively did the right thing: protecting their food from the bacteria that make it rot by handing it over to the care of good bacteria. In other words, they used bacteria to preserve their food. Every culture in the world includes traditional dishes that rely on the help of microbes for their preparation. Germany has its sauerkraut, pickled gherkins, and sourdough pretzels; the French love their crème fraîche; the Swiss have their hole-riddled cheese; salami and preserved olives come from Italy; Turks swear by a salty yogurt drink called ayran. None of these delicacies would exist if it weren't for microbes.

There are many, many examples from Asian cuisine: soy sauce, kombucha drinks, miso soup, Korean kimchi. Indians have lassi and Africans have fufu... the list is endless. All these foods rely on bacteria for a process we call fermentation. The process often results in the production of acid, which makes the yogurt or vegetables taste sour. This acid, along with the many good bacteria, protects the food from dangerous microbes. Fermentation is the oldest and healthiest way of preserving food.

The bacteria used in this technique were as varied around the world as the foods they helped to produce. The soured milk drunk in rural Germany was made using different bacteria from those used to make the ayran enjoyed in Anatolia. In the warmer countries of the south, bacteria were used that prefer to work under higher temperature conditions; in the chilly north, bacteria were chosen that like to do their job at room temperature.

Yogurt, soured milk, and other fermented products came about by accident. Someone left the milk outside, bacteria found their way into the churn (either directly from the cow or from the air during milking), the milk thickened, and a new kind of food had been invented. If a particularly delicious yogurt bacteria jumped into the mix, people added a spoonful of that yogurt to the next batch to make more of the same. Unlike today's yogurt products, however, traditional types were the work of whole teams of different bacteria—not just selected individual species.

The diversity of bacteria in fermented foods has fallen sharply. Industrialization has resulted in standardized production processes using

single bacteria species isolated in laboratories. Today, milk is briefly heated soon after it leaves the udder to kill off any potential pathogens, but this also kills any potential yogurt bacteria. That's why you can't just leave modern shop-bought milk to go sour in the hope that it will eventually turn into yogurt.

Many foods that used to be full of bacteria are now preserved using vinegar, as is the case with most pickled gherkins today. Some things are fermented using bacteria but then heated to kill off the microbes—shop-bought sauerkraut, for instance. Fresh sauerkraut is usually only sold in specialist health-food stores these days.

Scientists in the early twentieth century suspected that good bacteria were of great benefit to us. That is when Ilya Metchnikoff appeared on the yogurt scene. The Nobel Prize winner spent his time observing Bulgarian mountain peasants. He realized they often lived to be a hundred years old or more, and they were unusually contented. Metchnikoff suspected the key to their longevity lay in the leather bags they used to transport the milk from their cows. The peasants had to walk long distances, and their milk often turned sour or transformed into yogurt in the bags before they reached home. Metchnikoff became convinced that the secret to their long lives was their regular consumption of this bacterial product. In his book *The Prolongation of Life*, he asserted the claim that good bacteria can help us live longer, better lives. From then on, bacteria were no longer just anonymous components of yogurt, but important promoters of health. However, Metchnikoff's timing could hardly have been worse. Shortly before, it had been discovered that bacteria cause disease. Although the microbiologist Stamen Grigorov identified the bacterium described by Metchnikoff as *Lactobacillus bulgaricus* in 1905, he soon turned his efforts to the fight against tuberculosis. The successful use of antibiotics in fighting disease from around 1940 meant that the idea was fixed in most people's minds: the fewer bacteria, the better.

We have babies to thank for the fact that Ilya Metchnikoff's idea and Grigorov's *bacillus* eventually found their way onto our supermarket shelves. Mothers who were unable to breast-feed their babies found they often had a problem with their bottle-fed offspring. The babies were getting diarrhea much more often than they should. This took the formula-milk industry by surprise, because they had taken care to make sure their product

contained the same substances as real breast milk. What could be missing? The answer was, of course, bacteria. And, specifically, the bacteria that live on milky nipples and which are particularly common in the guts of breast-fed babies: *Bifidobacteria* and *Lactobacilli.* These bacteria break down the sugar in milk (lactose) and produce lactic acid (lactate), so they are classified as lactic-acid bacteria. A Japanese scientist used *Lactobacillus casei* Shirota to create a special yogurt, which mothers could initially buy only in pharmacies. When they fed it to their babies every day, the infants contracted diarrhea much less frequently. Industrial food research returned to Metchnikoff's idea—with baby bacteria and more modest aims.

Most normal yogurt contains *Lactobacillus bulgaricus*, although it is not necessarily precisely the same sort as that in the yogurt of the Bulgarian peasants. Today, the species discovered by Stamen Grigorov is more correctly known as *Lactobacillus helveticus* spp. *bulgaricus*. These bacteria are not particularly good at resisting digestion and only a small number of them reach the large intestine alive. That is not so important for some effects on the immune system—often just the sight of a few empty bits of bacteria wall is enough to prompt our immune cells into action.

Probiotic yogurt contains bacteria that researchers were inspired to use by the case of the bottle-fed babies with diarrhea. They are meant to reach the large intestine alive. Examples of bacteria that can resist being digested are *Lactobacillus rhamnosus*, *Lactobacillus acidophilus*, and the abovementioned *Lactobacillus casei* Shirota. The theory is that a living bacterium will have a greater effect on the gut. There are studies that show their effects, but they are not sufficient to satisfy the European Food Safety Authority. It has banned companies like Yakult and Danone from claiming their products promote health in their advertising.

These doubts are compounded by the fact that it is not always possible to know whether enough probiotic bacteria are reaching the large intestine alive. A break in the cold chain, or a person with a particularly acidic stomach or slow digestion, might kill off these microbes before they reach their intended destination. That is not harmful, of course, but it means consuming a probiotic yogurt may have no effect that a normal yogurt doesn't also have. To make any difference to the huge ecosystem in our gut, about a billion (109) bacteria need to make it through the system and arrive there intact.

To summarize: any yogurt can be good for you, although not everyone can tolerate milk protein or too much animal fat. The good news is that there is a world of probiotics beyond yogurt. Researchers are busy in their laboratories examining selected bacteria. They dribble bacteria directly onto gut cells in petri dishes, feed mice with microbial cocktails, or get volunteers to swallow capsules full of living microorganisms. Probiotic research has roughly defined three areas in which our good bacteria can display fascinating abilities.

1. Massaging and Pampering

Many probiotic bacteria take good care of our gut. They possess genes that enable them to produce small fatty acids like butyrate. This soothes and pampers the villi in the gut. Pampered villi are much more stable and likely to grow bigger than unpampered ones. The bigger the villi grow, the better they are at absorbing nutrients, minerals, and vitamins. The more stable they are, the less rubbish they let through. The result is that our body receives more nutrients and fewer damaging substances.

2. Security Service

Good bacteria defend our gut—it is, after all, their home and they do not willingly surrender their territory to bad bacteria. Sometimes they defend the gut by occupying the very places pathogens like to infect us most. When a bad bacterium turns up, it finds them sitting in its favorite spot with satisfied grins on their faces and their handbags on the seats next to them, leaving no room for anyone else to take up residence. Should that signal not be explicit enough—no problem! Security service bacteria have more tricks up their sleeves. For example, they can produce small amounts of antibiotics or other defensive substances that drive unfamiliar bacteria out of their immediate vicinity. Or they use various acids, which not only protect yogurt and sauerkraut from rotting bacteria, but also make our gut a less inviting environment for bad bacteria. Another trick is to snatch the bad bacteria’s food away (anyone with siblings may be familiar with this strategy). Some probiotic bacteria seem to have the ability to steal bad bacteria’s food from right under their noses. Eventually, the bad guys have had enough and give up.

3. Good Advice and Training

And, last but not least, the best experts in all things bacterial are bacteria themselves. When they work together with our gut and its immune cells, they provide us with insider information and useful advice. What do the different bacteria's outer walls look like? How much protective mucus is needed? What quantity of bacterial defense substances (defensins) should the gut cells produce? Does the immune system need to be more active in its reaction to foreign substances or should it sit back and accept newcomers?

A healthy gut contains many probiotic bacteria. We benefit every day and every second from their abilities. But sometimes our bacterial community faces attack. That can be from antibiotics, a bad diet, illness, stress, and

many, many other causes. Our guts are then less well cared for, less protective, and less good at giving advice. When that is the case, we can be thankful that some of the results of laboratory research have made it onto pharmacy shelves. Living bacteria are available that can be used like temporary workers brought in to help during times of heavy workloads.

Good for treating diarrhea. This is the number-one use for probiotics. Gastroenteritis (stomach flu) and diarrhea caused by taking antibiotics can be helped using various pharmacy-bought bacteria. They can reduce the length of such a bout of diarrhea by about a day. At the same time, unlike most diarrhea medications, they are almost free of side effects. That means they are particularly suitable for small children and old people. In conditions like ulcerative colitis and irritable bowel syndrome, probiotics can increase the intervals between diarrhea attacks or inflammatory flare-ups.

Good for the immune system. For people who tend to get sick often, it can be a good idea to try different probiotics, especially when colds are rife. If that is too expensive, eating a pot of yogurt a day may be enough, since bacteria don't necessary have to be alive to trigger some mild effects. Studies have shown that old people and high-performance athletes, in particular, are less prone to catching colds if they take probiotics regularly.

Possible protection against allergies. This is not as well documented as the effect of probiotics on diarrhea or a compromised immune system. Still, probiotics are a good option for parents of children with an increased risk of developing allergies or neurodermatitis. A large number of studies show they can offer significant protection. In some studies, the effect could not be proven, but that may be because each study used a different kind of bacterium. Personally, I think the "better safe than sorry" approach is appropriate here. Probiotics certainly do no harm to children with a high risk of developing allergies. Some studies showed an improvement in the symptoms of those already suffering from allergies or neurodermatitis.

As well as the well-researched areas like diarrhea, gastrointestinal disease, and the immune system, there are other areas that are only now undergoing scientific scrutiny. Digestive complaints, traveler's diarrhea, lactose intolerance, obesity, inflammatory joint disease, and diabetes are all promising areas of research.

If you ask your pharmacist to recommend a probiotic product to help with one of these problems (for example, constipation or flatulence), she will not be able to give you one that has been scientifically proven to work. The pharmaceutical industry and academic research are equally behind in this area. What remains for you is to try out different products for yourself until you hit upon a bacterium that seems to help. The packaging should always include the name of the bacteria the product contains. Try it for about four weeks and if you see no improvement, give a different bacterium a go. Some gastro-enterologists will advise you about the kind of bacteria that are more likely to be the ones you are looking for.

The rules are the same for all probiotics. You should try them for about four weeks and make sure they are still within the best-before date (otherwise sufficient bacteria may not have survived to have any effect on the huge ecosystem of the gut). Before buying probiotic products, you should find out whether they are intended by the manufacturer for the complaint you are hoping to treat. Different bacteria have different genes—some are better at advising the immune system, others are more belligerent about ridding the gut of diarrhea-causing bugs, and so on.

The best-researched probiotics to date are lactic-acid bacteria (*Lactobacilli* and *Bifidobacteria*) and *Saccharomyces boulardii*, which is a yeast. This yeast has not received the attention it deserves. It is not a bacterium, so it is not one of my favorites either, but it does have one huge advantage: as a yeast, it has absolutely nothing to fear from antibiotics.

So, while we are massacring our entire bacteria population by taking antibiotics, *Saccharomyces* can move in and set up house without a worry in the world. It can then protect the gut from harmful opportunists. It also has the ability to bind toxins. However, it does cause more side effects than bacterial probiotics. For example, some people have an intolerance to yeasts, which can cause them to break out in a rash.

The fact that almost all the probiotics we know—give or take a yeast or two—are lactic-acid bacteria shows how little we have yet discovered in this area. *Lactobacilli* are normally less common residents in the guts of adults, and *Bifidobacteria* are unlikely to be the only health-promoting microbes present in the large intestine. At the time of writing, there is only one other probiotic bacteria species that is as well researched as the two mentioned above: *E. coli* Nissle 1917.

This strain of *E. coli* was first isolated from the feces of a soldier returning from the Balkan War. All the soldier's comrades had suffered severe diarrhea in the Balkans, but he had not. Since then, many studies have been carried out to show that this bacterium can help with diarrhea, gastrointestinal disease, and a compromised immune system. Although the soldier died many years ago, scientists continue to breed his talented *E. coli* in medical laboratories and package it up for sale in pharmacies so it can work its wonders in other people's guts.

There is one limitation to the efficacy of all current probiotics we take: they are isolated species of bacteria bred in the lab. As soon as we stop taking them, they mostly disappear from our gut. Every gut is different and contains regular teams that help each other or wage war on each other. When somebody new turns up, they are at the back of the line when it comes to allocating places. So, currently, probiotics work like hair conditioner for the gut. When you stop taking them, the regular flora folk have to continue their work. To achieve longer-lasting results, researchers are now looking at the possibilities of a mixed-team strategy: taking several bacteria together, so that they can help each other to gain a foothold in unknown territory. They clear away each other's waste and produce food for their colleagues.

Some products you can buy at the pharmacy, drugstore, or supermarket already use this strategy, with a mix of our trusty old lactic-acid friends. And it seems they really do work better as a team. The idea that we might be able to encourage these bacteria to settle permanently in our gut is a nice one, but it has not yet been seen to work well... to put it mildly.

But if you persist doggedly with the teamwork strategy, it can have impressive results, for example, in treating *Clostridium difficile* infections. *Clostridium difficile* is a bacterium that can survive treatment with antibiotics and then colonize the entire area left free by the bacteria killed by treatment. Infected people often have bloody, slimy diarrhea for many years, which does not respond to further treatment with antibiotics or probiotics. This can put great strain not only on the body, but also on the mind.

In difficult situations like this, doctors really have to use all their creativity. A few brave medics have now begun transplanting experienced teams of bacteria, including all possible good and true gut bacteria, from the

guts of healthy donors to those with *Clostridium difficile* infections. Luckily, such a transplant is relatively easy to carry out (it has been used for decades by veterinary practitioners to cure many diseases). All you need are some healthy feces, complete with bacteria, and that's it. The treatment is known as fecal bacteriotherapy, or more directly, a fecal transplant. The feces used in medical fecal transplants are not pure, but they are purified. Then, it does not really matter whether they enter through the front or back door, so to speak.

Almost all studies show a success rate of around 90 percent in treating previously incurable diarrhea caused by *Clostridium difficile*. Few medical drugs have such a high success rate. Despite these positive results, the treatment can currently be used only on patients with truly hopeless cases of incurable diarrhea. The danger is that other diseases or potentially harmful bacteria might be transplanted along with the donor stool. Some companies are already working to develop artificial stool that they can guarantee is free of any harmful elements. If they succeed, the therapy is likely to become much more widespread.

Probiotics' greatest potential probably lies in transplanting beneficial bacteria to the gut, where they would settle permanently and grow. Such transplants have already helped patients with severe diabetes. Scientists are currently investigating whether they can also be used to prevent patients from ever developing full-blown type 1 diabetes.

The connection between stool and diabetes may not be immediately obvious to everyone. But, in fact, it is not as absurd as it seems. It is not just defensive bacteria that are transplanted with the stool, but an entire microbial organ that plays an important part in regulating the body's metabolism and immune system. We are still completely ignorant of more than 60 percent of these gut bacteria. Looking for species that may have probiotic effects is time-consuming and difficult, just as the search for medicinal plants was in the past. Only this time, the search is going on inside us. Every day we live and every meal we eat influence the great microbial organ inside us—for better or for worse.

Prebiotics

The central idea surrounding the use of prebiotics is to support our good bacteria by eating certain foods. Prebiotics are much more suitable for daily use than probiotics. To gain the benefits they offer, just one condition must be met: good bacteria must already be present in the gut. These can then be encouraged by eating prebiotic food, which gives the good bacteria more power over any bad bacteria that may also be present.

Since bacteria are so much smaller than we are, they view food from a very different perspective from our own. Every little grain becomes a major event, a comet of deliciousness. Food we cannot digest in the small intestine is called dietary fiber or roughage. But, despite the name, it is not rough on the bacteria of the large intestine. Quite the opposite, in fact: they love it! Not all kinds, but some, anyway. Some bacteria love undigested asparagus fibers, while others prefer undigested meat fibers.

Some doctors who recommend their patients eat more dietary fiber do not even really know the reason, which is that they are prescribing a hearty meal for your bacteria that will benefit you, too. Finally your gut microbes get enough to eat, so they can produce vitamins and healthy fatty acids or put the immune system through a good training session. However, there are always some pathogens among the bacteria in our gut. They can use certain foodstuffs to produce substances like indole, phenols, or ammonia. Those are the substances you find in the chemistry cupboard with a warning symbol on the bottle.

This is exactly how prebiotics can help: they are roughage that can only be eaten by nice bacteria. If such a food were available in the human world, the lunch room at work would be quite an eye-opener! Household sugar is not a prebiotic, for example, because it is also a favorite of tooth-decay bacteria. Bad bacteria cannot process prebiotics at all, or hardly, and so they cannot use prebiotics to produce their evil chemicals. At the same time, good bacteria fed with prebiotics grow constantly in power and can gain the upper hand in the gut.

Artichoke, asparagus, endive, green bananas, Jerusalem artichoke, garlic, onion, parsnips, black salsify, wheat (wholegrain), rye, oats, leek.

And it is not even very hard to do yourself and your best microbes a favor with prebiotics. Most people already have a favorite prebiotic dish that they would not mind eating more often. My granny always has some potato salad in her fridge, my dad's specialty is a great endive salad with mandarin segments (here's a tip: rinse endive leaves briefly under warm water—this leaves them crispy but removes some of the bitterness), and my sister can't resist asparagus or black salsify in a creamy sauce.

Those are just a few dishes that *Bifidobacteria* and *Lactobacilli* love to eat. We now know that they prefer vegetables from the lily family (*Liliaceae*), which includes leeks and asparagus, onions, and garlic. They also like *Compositae* plants, which are those from the sunflower family,

including endives, salsify, artichokes, and Jerusalem artichokes. Resistant starches are also on their list of favorites.

Resistant starches form, for example, when potatoes or rice are boiled and then left to cool. This allows the starches to crystalize, making them more resistant to digestion. This means that more of your potato salad or cold sushi rice reaches your microbes untouched. If you don't already have a favorite prebiotic dish, give them a try. Eating these dishes regularly has an interesting side effect—it causes regular cravings for just such foods.

People who eat mainly low-fiber foods like pasta, white bread, or pizza should not suddenly switch to eating large portions of high-fiber foods. That will only overwhelm their under-fed bacterial community. The sudden change will freak the bacteria out, and they will metabolize everything they can in a fit of euphoria. The result is a never-ending trumpet concerto from down below. So, the best strategy is to gradually increase the amount of dietary fiber and not to feed your bacteria with massive, unmanageable amounts. After all, the food we eat is still first and foremost for us, and only secondarily for the inhabitants of our large intestine.

Overproduction of gas is not a pleasant thing—it bloats the gut, making us feel uncomfortable—but passing a bit of wind is not only necessary, it is healthy, too. We are living creatures with a miniature world living inside us, working away and producing many things. Just as we release exhaust fumes into the Earth's atmosphere, so must our microbes, too. It may make a funny sound and it may smell a bit, but not necessarily. *Bifidobacteria* and *Lactobacilli,* for instance, do not produce any unpleasant odors. People who never need to break wind are starving their gut bacteria and are not good hosts for their microbe guests.

Pure prebiotics can be bought at the pharmacy or drugstore. These include the prebiotic inulin, which is extracted from endives, and GOS (galacto-oligosaccharides), which are isolated from milk. These substances have been tested for their health-giving effects and are pretty efficient at feeding only certain *Bifidobacteria* and *Lactobacilli.*

Prebiotics are nowhere near as well researched as probiotics, although there are already some sound results pertaining to how they work. Prebiotics promote good bacteria, resulting in a reduction in the amount of toxins produced in the gut. People with liver problems, especially, are unable to detoxify these substances well, and that can cause serious

problems. Bacterial toxins have various effects on the body, including anything from fatigue and tremors to comas. When such patients are treated in hospital, they are often given highly concentrated prebiotics, which usually leads to a disappearance of their symptoms.

But bacterial toxins also influence Joe Blow with his fully functioning liver. Toxins can develop, for example, if Joe eats too little dietary fiber and the fiber is all used up at the beginning of his large intestine. The bacteria at the end of his gut will then pounce on any undigested proteins. Bacteria and meat can be a bad combination—we know it's never a good idea to eat rotten meat. Too many meat toxins can damage the large intestine and, in a worst-case scenario, can even cause cancer. The end of the gut is more prone to cancers on average than the rest of the organ. That's why researchers are so keen to test how well prebiotics can protect against cancer. Early results are promising.

Prebiotics like GOS are interesting because they are also produced by our own bodies. Ninety percent of the roughage in human breast milk is GOS, and the remaining 10 percent is made up of other indigestible fiber. In cow's milk, GOS accounts for only 10 percent of the fiber content. So it appears there is something about GOS that is important for human babies. If bottle-fed babies are given formula milk that contains a little GOS powder, their gut bacteria looks similar to that of breast-fed babies. Some studies indicate that they are less prone to allergies and neurodermatitis in later life than other bottle-fed babies. GOS has been approved as an additive to infant milk formula for a few years, but it is not obligatory.

Since then, interest in GOS has increased, and another of its effects has now been demonstrated in the laboratory. GOS docks onto gut cells directly —preferably at locations otherwise favored by pathogens. That means these prebiotics act as microscopic shields. Bad bacteria cannot get a good hold and are more likely to slip and fall away. These results have prompted new studies into GOS as a way of preventing traveler's diarrhea.

More research has been carried out into inulin than GOS. Inulin is sometimes used as a sugar or fat substitute in the food industry because it is a little bit sweet and has a gel-like consistency. Most prebiotics are sugars that are linked into chains. When we speak of sugar, we often mean a particular molecule extracted from sugar beet or sugar cane, but there are more than a hundred different kinds of sugar. If, historically, we had

developed a sugar industry based on endive sugar, our sweets would not cause tooth decay. Sweetness is not in itself unhealthy, we simply eat only the most unhealthy kind of sweetness.

We are often skeptical about products that are labeled sugar-free or low fat. Sweeteners like aspartame appear to be carcinogenic, and other substances used in typical diet products are also used in factory farming to fatten pigs. So our skepticism is justified. But a product that contains inulin as a sugar or fat substitute may well be healthier than one with a full dose of animal fat or sugar. It is worth reading the label on diet products closely because we can consume some of them with a clean conscience and our gut microbes will thank us for it, too.

Inulin cannot bind with our cells as well as GOS. A large and well-run study in the United Kingdom showed it did not offer any protection against traveler's diarrhea, although the test subjects did report a general improvement in well-being after taking inulin. This pleasant effect was not reported by members of the control group, who were given a placebo. Inulin can be produced with different chain lengths, which is great for attaining a beneficial distribution of good bacteria. Short inulin chains are eaten by the bacteria at the start of the large intestine and longer chains are consumed closer to the end.

The so-called ITF_{MIX} containing chains of differing lengths has good results, where more surface area equals better results, for example in the absorption of calcium, which requires bacteria to pass it through the gut wall. In one experiment, ITF_{MIX} was seen to improve calcium absorption in young girls by up to 20 percent. That is good for the bones and can help protect against osteoporosis in old age.

Calcium is such a good example because it shows the limits of what can be achieved with prebiotics. Firstly, you have to ingest enough calcium for an effect to kick in, and secondly, prebiotics can do nothing if the problem lies with other organs. When many women go through menopause, their bones get weaker. This is due to a mid-life crisis in the ovaries. They have to say goodbye to their life of producing hormones and learn how to enjoy their retirement. But the bones miss those hormones! No prebiotic in the world can help with this kind of osteoporosis.

Nevertheless, we should not underestimate the power of prebiotics. Almost nothing influences our gut bacteria as much as the food we eat. Prebiotics are the most powerful tool at our disposal if we want to support our good bacteria—that is, those that are already there and are there to stay. Prebiotic creatures of habit, like my potato salad–addicted granny, are doing the best part of their microbial organ a favor without even knowing it. Incidentally, her second favorite vegetable is leeks. Whenever everyone else was ill, she would be there with a big smile and some soup, merrily playing us a few songs on the piano. I don't know if her defenses had anything to do her microbes, but it's not an illogical conclusion.

So, we should remember: good bacteria do us good. We should feed them well so they can populate as much of our large intestine as possible. Pasta and bread made of white flour on factory production lines are not enough. We need to include real roughage, made of real dietary fiber in vegetables and fruit. This roughage can also satisfy a sweet tooth and taste delicious. It can be fresh asparagus, sushi rice, or pure, isolated prebiotics from the pharmacy. Our bacteria will like it, and they will thank us with their good services.

SEEN UNDER THE microscope, bacteria look like nothing but little, bright spots against a dark background. But taken together, their sum is much greater than their parts. Each one of us hosts an entire population. Most sit in our mucus membrane, diligently training our immune system, soothing our villi, eating what we don't need, and producing vitamins for us. Others keep close to the cells of the gut, needling them or producing toxins. If the good and the bad are in equilibrium, the bad ones can make us stronger and the good ones can take care of us and keep us healthy.

Acknowledgments

THIS BOOK WOULD not exist if it weren't for my sister, Jill. Without your free, rational, and inquisitive mind, I would have been stuck many times in a world where obedience and conformity are easier than courage and the will to make necessary mistakes. Although you lead a busy life yourself, you were always there, ready to go through my texts with me and inspire me with new ideas. You taught me how to work creatively. Whenever I feel bad, I remember we are made of the same stuff and each of us uses her talents differently. I would like to thank Ambrosius, who shielded me from too much work with a protective arm. I would also like to thank my family and my godfather for surrounding me like a forest surrounds a tree, keeping me rooted even when strong winds are blowing. I also thank Ji-Won for keeping me nourished so often during the writing of this book—with food and her wonderful nature. My thanks go to Anne-Claire and Anne for their help with even the trickiest of questions!

I thank Michaela and Bettina, without whose sharp minds the writing of this book would never have come about. If it weren't for my medical studies I would never have had the knowledge necessary to write this book, so I thank all my good teachers and professors, as well as the German state, which pays for my university studies. To everyone who has contributed their hard work to the realization of this book—from press officers, publishers, manufacturers, printers, marketers, proofreaders, booksellers, postal workers, to those of you reading this now: Thank you!

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THIS LIST MAINLY contains references to sources dealing with content not normally covered in the standard text books.

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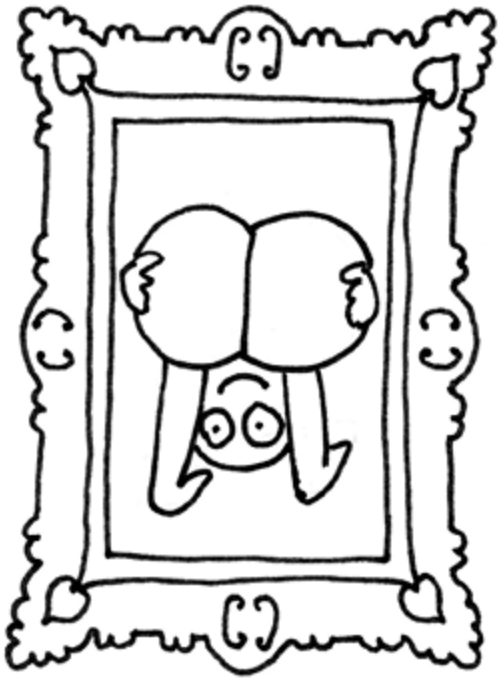
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